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Specific Markers for Pancreatic Cancer

comprising at least one polypeptide identified by proteomics to be up-regulated in pancreatic cancer, to an in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of a) obtaining a biological herein. Furthermore, screening methods relating to antagonists of the specific markers sample; and b) detecting and/or measuring the increase of specific markers as disclosed The present invention relates to markers for diagnosis of pancreatic cancer disclosed herein are provided.

Among the causes for this late presentation is the lack of diagnostic methods for an patients with pancreatic cancer, accurate preoperative diagnosis is difficult to achieve with conventional imaging analyses. Most patients with pancreatic cancer present late in earlier detection of the disease. Besides this lack of diagnostic methods, the high mortality Pancreatic cancer is a common cause of death in the Western world. It is one of the only up to 20% are candidates for resection and have the potential for curative surgery. Therefore, the identification of new targets for early diagnosis of pancreatic tumors, and most aggressive malignant tumors, with an overall 5-year survival rate of 0.496. In many the course of the disease and have either locally extensive or metastatic disease. Overall, of patients with pancreatic cancer is additionally caused by a lack of effective treatments. for the development of agents to treat pancreatic cancer is a challenge of paramount ន

for early diagnosis of the disease, and the long felt need for such markers, was overcome by the present invention by applying the new technology of proteomics. It was surprisingly found by using proteomic technology that a specific set of polypeptides are differentially expressed in pancreatic tissue obtained from individuals suffering from The problem of identifying polypeptides suitable as markers of pancreatic cancer HR/03.11.2003 2

used as markers for diagnosis of pancreatic cancer. The invention also provides an in vito method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the sueps of a) obtaining a biological sample; and b) detecting and/or measuring the increase of one or more polypepides as disclosed herein. Purthermore, screening methods relating to inhibitors and (57) Abstract: The present invention provides polypeptides which are up to cancer and/or the invention provides polypeptides which are up to cancer and/or the susceptibility to pencreatic cancer. The invention also polypeptides as disclosed herein.

provides polypeptides which are up- or down-regulated in pancreatic cancer and which can be

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encoded by genes which were previously identified to be up-regulated in pancreatic polypeptides are listed in appended tables 2 and 3. The polypeptides in table 3 are pancreatic cancer, as compared to healthy pancreatic tissue. Said differentially expressed cancer on the transcriptional level (Iacobuzio-Donahue et al., (2002), Am. J. Pathol. 160, 1239-1249). However, it is well known that regulation on the transcriptional level is not necessarily indicative of a similar regulation of the expression of the respective gene on the translational level. Thus, only by demonstrating that the polypeptides listed in table 3 are up-regulated in pancreatic cancer is it possible to use them for polypeptide-based diagnostic assays for the detection of pancreatic cancer.

consisting of Seq ID No. 3, 4, 6, 9, 14, 15, 27, 31 to 35, 37, 39, 40; and/or Seq ID No. 50 to 52. Even more preferably, said polypeptides are selected from the group consisting of Seq from the group consisting of the polypeptides listed in tables 2 and/or 3 (Seq ID No. 1 to cancer. Preferably, said polypeptides are selected from the group consisting of Seq. ID No. 2 to 10, 12 to 15, 17, 19, 20, 23, 24, 27, 28, 31 to 40, 42 to 45, 47 and 48; and/or Seq ID No. 25 and 50 to 54. More preferably, said polypeptides are selected from the group Based on the polypeptides listed in tables 2 and 3, the present invention provides a marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected 24 and 26 to 49; and/or Seq ID No. 25 and 50 to 55). Thus, the term "marker" as used herein refers to one or more polypeptides that are regulated in cancer and that can be used to diagnose pancreatic cancer or a susceptibility to pancreatic cancer either alone or as combinations of multiple polypeptides that are known to be regulated in pancreatic ID No. 4, 6, 9, 14, 15, 31, 33 to 35 and/or Seq ID No. 51 and 52. Most preferably, said polypeptides are selected from the group consisting of Seq ID No. 4, 6, 14, 15 and 31; and/or Seq ID No. 52.

The term "polypeptide" as used herein, refers to a polymer of amino acids, and not to a specific length. Thus, peptides, oligopeptides and proteins are included within the definition of polypeptide. Preferably, the marker of this invention is a marker comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 2.

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19, 20, 23, 24, 27, 28, 31 to 40, 42 to 45, 47 and 48 from table 2 and/or Seq ID No. 25 and 50 to 54 from table 3. These polypeptides are induced at least two fold, as can be seen in tables 2 and 3. More preferably, said polypeptides are selected from the group consisting of Seq ID No. 3, 4, 6, 9, 14, 15, 27, 31 to 35, 37, 39, 40 from table 2 and/or Seq ID No. 50 to 52 from table 3. These polypeptides are induced at least three fold, as can be seen in and 52 from table 3. These polypeptides are induced at least 4 fold, as can be seen in tables 2 and 3. Most preferably, said polypeptides are selected from the group consisting listed in tables 2 and/or 3, is used as a marker or as part of a marker for diagnosis of polypeptides are selected from the group consisting of Seq. ID No. 2 to 10, 12 to 15, 17, tables 2 and 3. Even more preferably, said polypeptides are selected from the group consisting of Seq ID No. 4, 6, 9, 14, 15, 31, 33 to 35 from table 2 and/or Seq ID No. 51 of Seq ID No. 4, 6, 14, 15 and 31 from table 2 and/or Seq ID No. 52 from table 3, which Furthermore, a polypeptide selected from the group consisting of the polypeptides pancreatic cancer and/or the susceptibility to pancreatic cancer. Preferably, said are the polypeptides that are induced five fold, as shown in tables 2 and 3. 2

The present invention pertains to a marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 6. Preferably, said at least one polypeptide additionally does not include Seq ID No.s 25 and 50 to 55. In a preferred embodiment, the marker hereinbefore described additionally comprises at least one of the polypeptides listed in table 5.

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Several groups of polypeptides were identified as markers for pancreatic cancers:

One of the enzymes that caught our attention was Glutamine y-

translational modification (cross-linking and conjugation with polyamines) of proteins at glutamyltransferase/tissue transglutaminase (TGLC, Seq ID No. 54). It is a member of the transglutaminase family that catalyzes Ca2+ dependent reactions resulting in the post

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the level of glutamine and lysine residues (Greenberg, C. S., Birckbitchler, P. J., and Rice, R. H. Transglutaminases: multifunctional cross-linking enzymes that stabilize tissues. FASEB J., 5: 3071-3077, 1991). Many different roles for this protein have been described, among them apoptosis, adhesion, and differentiation (Amendola, A., Pesus, L.,

- Piacentini, M., and Szondy, Z. "Tissue" transglutaminase in AIDS. J.Immunol.Methods, 265: 145-159, 2002). There is some controversy on the role of TGLC in apoptosis. While several pieces of evidence suggest that TGLC is a pro-apoptotic protein (Melino, G., et al., Mol.Cell Biol., 14: 6584-6596, 1994), Jason et al. found that TGLC acts in anti-apoptotic fashion (Boehm, J. E., et al. J.Biol.Chem, 277: 20127-20130, 2002). Many substrates of
 - 10 TGLC are major extra-cellular matrix (ECM) components such as fibronectin, osteonectin, and collagen, which makes TGLC an important enzyme in ECM development (Raghunath, M., et al., J.Clin.Invest, 98: 1174-1184, 1996., Nemes, Z., Jr., et al. J.Biol.Chem., 272: 20577-20583, 1997). Abnormal ECM development is involved in many pathological conditions such as fibrosis and may play a role in the proliferation of fibrous tissue observed in PC. Haroon et al. described that TGLC ECM-promoting abilities are an important part of the host response mechanism against tumor growth (Haroon, Z. A., et al., Lab Invest, 79: 1679-1686, 1999). Interestingly, loss of TGLC can be a biomarker for prostate adenocarcinoma (Birckbitchler, P. J., et al., Cancer, 89: 412-423, 2000), which raises the question whether the measured TGLC is produced by neoplastic
 - 2000), which raises the question whether the measured TGLC is produced by neoplastic ductal cells and/or stromal cells. Measurements of mRNA levels in PC, normal tissue and PC cell lines indicate that TGLC is over expressed in both cell types (lacobuzio-Donahue, C. A., et al., Am.J.Pathol., 160: 1239-1249, 2002), which would distinguish PC from prostate adenocarcinoma. Therefore, one preferred embodiment of the present invention is a marker comprising Seq ID No. 54.

Cytoskeletal proteins

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Several cytoskeletal proteins were detected at higher levels in PC than in surrounding tissue. One of these is gelsolin (Seq ID No. 3), a Ca²⁺ and PIP2 (polyphosphoinositide 4,5-bisphosphate) regulated severing and capping protein, which is a multifunctional actin regulatory protein and has roles in actin remodeling, motility, signaling, apoptosis and cancer (Maruta, H. G proteins cytoskeleton and cancer. Austin, Tex: R.G. Landes, 1998). In several cancer studies, gelsolin expression has been described as down-regulated during carcinogenesis (breast, colon, stomach, bladder, prostate, and lung) (Asch, H. L., et al., Cancer Res., 56: 4841-4845, 1996; Dosaka-Akita, H., et al., Cancer Res., 58: 322-327, 1998, Prasad, S. C., et al. Electrophoresis, 18: 629-637, 1997). Another example for an up-regulated cytoskeletal protein is fascin (Seq ID No. 58), an

actin-bundling protein that has a role in cell matrix adhesion, cell interaction and migration. Fascin over expression has been reported in several cancers, such as breast, colon, and ovarian carcinoma (29). The present invention also features fascin 2 as a polypeptide up-regulated in pancreatic cancer (Seq ID No. 56). Thus, a preferred embodiment of the present invention is a marker comprising Seq ID. No. 3. In another preferred embodiment, the marker comprises Seq. ID No. 58. In another preferred embodiment, the marker comprises Seq. ID No. 58. In another preferred embodiment, the marker comprises Seq. ID No. 56.

In our study, cytokeratin 7 (Seq. ID No. 52) and cytokeratin 19 (Seq ID No. 33) showed strong expression in PC. Both have also been described in other cancers and have been linked with metastasis formation (Moll, R., Int.] Biol.Markers, 9: 63-69, 1994.). High protein levels of actinin-4 (Seq ID No. 5) were detected in PC. This protein was linked by others with cell motility and cancer invasion (Honda, K., Yamada, T., Endo, R., Ino, Y., Gotoh, M., Tsuda, H., Yamada, Y., Chiba, H., and Hirohashi, S. J.Cell Biol., 140. 1383-1393, 1998.). Taken together, the apparent strong expression of cytoskeletal proteins is likely to be an important factor in the strong invasiveness and metastasisforming potential of PC. Thus, a preferred embodiment of the present invention is a marker comprising Seq ID. No. 52. In another preferred embodiment, the marker comprises Seq. ID No. 33. In another preferred embodiment, the marker comprises Seq. ID No. 33. In another preferred embodiment, the marker comprises Seq. ID No. 34. In another preferred embodiment, the marker comprises Seq. ID No. 35. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 39. In another preferred embodiment, the marker comprises Seq. ID No. 30. In another preferred embodiment, the marker comprises Seq. ID No. 30. In another preferred embodiment, the marker comprises Seq. ID No. 30. In another preferred embodiment, the marker comprises Seq. ID No. 30. In another preferred embodiment and the seq. 200

Metastasis

Cancer of exocrine pancreas is characterized by extensive local invasion, early lymphatic and hematogenous metastasis. Metastasis in PC has been found in the skeleton, eye, bladder, etc. The extent of angiogenesis depends on the balance between pro-angiogenic activity from cancer and host cell. Currently, intratumoral microvessel density (IMD) measured by immunocytochemistry appears to be the most reliable parameter for assessing angiogenic activity. Patients with high IMD have decreased survival rates in a variety of cancers (Fujioka, S., et al., Cancer, 92. 1788-1797, 2001). Thymidine phosphorylase (TYPH or TP, Seq ID No. 31) which is identical to platelet-derived endothelial cell growth factor, is strongly expressed in PC and stimulates the chemotaxis of endothelial cells through the 2-deoxy-D-ribose, degradation products of thymidine by TP, thus indirectly inducing angiogenesis (Haraguchi, M., et al. Nature, 368: 1994.). Shuichi Fujioka et al. found that IMD and TP status were independent predictive indicators for overall as well as relapse-free survival in PC (Fujioka, S., et al., Cancer, 92: 1788-1797, 2001). An additional protein detected at higher levels in PC than in surrounding tissue likely involved in metastasis formation is

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osteoblast specific factor 2 (Seq ID No.53), a putative bone adhesion protein. Breast carcinoma commonly metastasizes to bone (Guise, T. A. Cancer, 88: 2892-2898, 2000). Although the role of this protein in PC is not clearly established, our findings suggest a similar role for osteoblast specific factor 2 in PC. Thus, a preferred embodiment of the present invention is a marker comprising Seq ID. No. 31. In another preferred embodiment, the marker comprises Seq. ID No. 53.

Small GTP-binding proteins

transactivation and was shown to be overexpressed in prostate cancer (Sampson, E. R., et constitute a superfamily, which is structurally classified into at least five families: the Ras, expression, cytoskeletal reorganization, and nucleocytoplasmic transport (Takai, Y., et al. Physiol Rev., 81: 153-208, 2001). RAN is known to enhance androgen receptor-mediated 81% of prostate tumor cases, may contribute to over proliferation of prostate tumor cells important role in angiogenesis and cancer growth. Berns et al, found GBLP up-regulated GBLP (guanine nucleotide binding protein \(\beta\) subunit-like protein RACK1, Seq. ID No. al., J.Biol. Regul. Homeost. Agents, 15: 123-129, 2001). Increased expression of RAN in expressed in PC than in normal pancreas tissue. These include RAN (Seq. ID No. 27), 47), GDIR (Rho GDP dissociation inhibitor 1, Seq. ID No. 55), and IQG1 or IQGAP1 activated protein kinase CB and a variety of other proteins. Protein kinase C plays an angiogenically active tissue (Berns, H., et al., FASEB J., 14: 2549-2558, 2000). Further Four small GTP-binding proteins and interacting proteins were more strongly (Li, P., et al., Am J Pathol., 161: 1467-1474,2002). GBLP is an anchoring protein for (Ras gtpase activating like protein, Seq ID No. 25). Small GTP-binding proteins Rbo, Rab, Sar1/Arf, and Ran families and are involved in the regulation of gene more, mRNA expression of GBLP is detected in epithelial cells of human colon in during angiogenesis in vitro and also associated with nonendothelial cells in

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phenotype in gastric cancer (Sugimoto, N., et al., I. Hum. Genet., 46: 21-25, 2001). By immunohistochemical analysis, IQGAP1 was found overexpreased in colorectal carcinoma and associated with carcinoma invasion (Nabeshima, K., et al., Cancer Lett., 176: 101-109, 2002). Since cancer invasiveness is associated with the localized diaruption of cell-cell adhesion, both our results and Iacobuzio-Donahue et al.'s data suggest that IQGAP1 may be involved in the disruption of local adhesion and in PC invasion to surrounding tissue. Thus, a preferred embodiment of the present invention is a marker comprising Seq ID No. 27. In another preferred embodiment, the marker comprises Seq ID No. 47. In another preferred embodiment, the marker comprises Seq ID No. 55. In another preferred embodiment, the marker comprises Seq ID No. 55. In another preferred embodiment, the marker comprises Seq ID No. 55. In another preferred embodiment, the marker comprises Seq. 10 No. 25.

S100 protein family

mucosa, as shown by proteomics analysis (Stulik, J., et al., Electrophoresis, 20: 1047-1054, Frends Biochem.Sci., 21: 134-140, 1996). S100A8 and S100A9 are negatively regulated by carcinogenesis (Gebhardt, C., et al., Oncogene, 21: 4266-4276, 2002). These proteins are 1999). S100A9 has been detected in cultured human adenocarcinoma (AC) cells derived diseases) (Donato, R. Int.J.Biochem.Cell Biol., 33; 637-668, 2001). S100A8 and S100A9 adenocarcinoma (Arai, K., et al., Oncol.Rep., 8: 591-596, 2001). Iacobuzio-Donahue et 2002). Thus, a preferred embodiment of the present invention is a marker comprising heumatoid arthritis, cystic fibrosis, psoriasis, allergic dermatitis, inflammatory bowel differentiation and DNA hypomethylation (Rosty, C., et al., Am.J.Pathol., 160: 45-50, also more strongly expressed in colorectal carcinoma than in matched normal colon endothelial origin and accumulation at sites of acute and chronic inflammation (e.g. intracellular as well as extracellular functions (Schafer, B. W. and Heizmann, C. W. glucocorticoids in a c-Fos-dependent manner and over expressed throughout skin Another protein with high-level expression in PC is \$109 (\$100A9, MRP-14, an form a noncovalent heterodimer protein complex called calprotectin. Current from various organs, and is associated with tumor differentiation in pulmonary al's work indicates that over expression of S100A4 in PC is associated with poor characterized by cell type-specific expression in cells of epithelial, myeloid and homologous low molecular weight calcium binding proteins. Calgranulins are reports support that both of \$100.A9 and \$100 A8 have wide range of possible calgranulin B, Seq ID No. 49), a member of the S100 protein family of highly 2

Innerin

that interacts with F-actin in vivo and that can cross-link P-actin microfilaments in vitro.

protein) is a widely expressed 190-kDa Cdc42-, Rac1-, and calmodulin-binding protein

block apoptotic signal pathway mediated by Ras and c-jun kinase, resulting in the increase resistance against environmental stress. IQG1 (Ras GTPase-activating-like

carcinoma and proliferating epithelial cell of normal colon tissue. Therefore, there is a

likely link between high GBLP expression and tumor growth. GDIR (Rho GDP

dissociation inhibitor) had been found up-regulated in a chemoresistant fibrosarcoma cell line by 2D-PAGE (Sinha, P., et al., Electrophoresis, 20: 2961-2969, 1999) and may IQGI negatively regulates the Ecc-based (B-cadherin/catenin complex) cell-cell adhesion by dissociating alpha-catenin. Up-regulation of IQGAP1 is correlated with the malignant

- 8 -We found that annexin 1 (Seq ID No. 51) and annexin 2 (Seq ID No. 19) have high

level of expression in PC. Both are members of a family of Ca²⁺-dependent membrane-binding proteins. Described functions include, among others, an important role in malignant transformation (Masaki, T., et al., Hepatology, 24: 72-81, 1996), the control of

s epithelial cell line proliferation (Solito, E., et al., Cell Growth Differ., 9, 327-336, 1998), and mediation of apoptosis (Canaider, S., et al., Life Sci., 66: L265-L270, 2000). Evidence in support of causative roles for any annexins in the development of cancer is still mainly circumstantial. In MCF-7 breast carcinoma cells, overexpression of annexin 1 led to

abrogation of Ca2+ release after activation of purinergic or bradykinin receptors (Frey, B. 10 M., et al., FASEB J., 13: 2235-2245, 1999), while over expression of annexin1 in rat 2 fbroblasts leads to direct inhibition of cytosolic PLA2, which in turn depresses the serum

fibroblasts leads to direct inhibition of cytosolic PLA2, which in turn depresses the serum response element of c-fos (Oh, J., et al., FEBS Lett., 477: 244-248, 2000). Collectively, these studies imply a growth-suppressive role for annexin1. These results are not supported by the finding that annexin 1 is strongly up-regulated in a prostate cancer cell

line (Vaarala, M. H., Lab Invest, 80: 1259-1268, 2000), esophageal cancer (Emmert-Buck, M. R., et al., Mol.Carcinog, 27: 158-165, 2000), a stomach cancer cell line (Sinha, P., et al., J. Biochem. Biophys. Methods, 37: 105-116, 1998), mammary adenocarcinoma (Pencil, S. D. and Toth, M. Clin. Exp. Metastasis, 16: 113-121, 1998), and hepatocarcinoma (de Coupade, C., et al., Hepatology, 31: 371-380, 2000). In hepatocarcinoma, study also

showed that the proliferative rate of both normal and malignant hepatocytes was attenuated by antisense to annexin 1. These and our data suggest that cell growth is associated with elevated rather than reduced levels of annexin 1, which is also supported by the studies of Iacobuzio- Donahue et al. (Am. J. Pathol., 160: 1239-1249, 2002). Thus, a preferred embodiment of the present invention is a marker comprising Seq ID No. 51.

25 In another preferred embodiment, the marker comprises Seq. ID No. 19.

Some additional proteins highly expressed in PC may have either clear roles in PC or an indirect link with PC, e.g. BGH3 (TGF-\beta1-induced protein, Seq ID No. 6) which is a secretory protein and acts as a marker for biologically active TGF-\beta 1 (Langham, R. G., et al., Transplantation, 72: 1826-1829, 2001). Thus, a preferred embodiment of the present invention is a marker comprising Seq ID No. 6.

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and detecting and/or measuring the increase of a marker described hereinbefore. The invention provides an in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of obtaining a biological sample; term "detection" as used herein refers to the qualitative determination of the absence or presence of polypeptides. The term "measured" as used herein refers to the quantitative determination of the differences in expression of polypeptides in biological samples from Antibodies recognizing the polypeptides listed in table 2, 3, 5 and/or 6 can either be generated for the purpose of detecting said polypeptides, eg. by immunizing rabbits with With the identification of polypeptides regulated in pancreatic cancer, the present patients with pancreatic cancer and biological samples from healthy individuals. Methods purified proteins, or known antibodies recognizing said polypeptides can be used. For example, an antibody capable of binding to the denatured proteins, such as a polyclonal antibody, can be used to detect the peptides of this invention in a Western Blot. An example for a method to measure a marker is an ELISA. This type of protein quantitation or absence of the markers of this invention. Methods for the detection of these markers are well known in the art and include, but are not limited to, immunohistochemistry or immunofluorescent detection of the presence or absence of the polypeptides of the mentioned hereinbefore are described in Harlow, E. and Lane, D. Antibodies: A for detection and/or measurement of polypeptides in biological samples are well known is based on an antibody capable of capturing a specifc antigen, and a second antibody capable of detecting the captured antigen. A further method for the detection of a diagnostic marker for pancreatic cancer is by analysing biopsy specimens for the presence marker of this invention. Methods for preparation and use of antibodies, and the assays in the art and include, but are not limited to, Western-blotting, ELISAs or RIAs Laboratory Manual, (1988), Cold Spring Harbor Laboratory Press. 2 13

The accuracy of the diagnosis of pancreatic cancer can be increased by analysing combinations of multiple polypeptides listed in tables table 2, 3, 5 and/or 6. Thus, the in vitro method herein before described, comprises a marker which comprises at least two, preferably at least three, more preferably at least four, even more preferably at least five, and most preferably at least six of the polypeptides listed in table 2,3, 5 and/or 6.

For diagnosis of pancreatic cancer, suitable biological samples need to be analysed for the presence or absence of a marker, Said biological samples can be serum, plasma,

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pancreatic juice or cells of pancreatic tissue. Cells from pancreatic tissue can be obtained by ERCP, secretin stimulation, fine-needle aspiration, cytologic brushings and large-bore needle biopsy It is also possible to diagnose pancreatic cancer by detecting and/or measuring nucleic acid molecules coding for the marker hereinbefore described. Preferably, said nucleic acid molecule is RNA or DNA. In another embodiment, said DNA is a cDNA. In one embodiment of the present invention, the in vitro method herein before described comprises comparing the expression levels of at least two of the nucleic acids encoding said polypeptides in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer, to the expression levels of the same nucleic scids in a healthy individual.

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embodiment of the in vitro method, an increase or decrease of the expression levels of suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer to the expression levels of the same marker in a healthy individual. In a more preferred In another embodiment of the present invention the in vitro method herein before described comprises comparing the expression level of said marker in an individual said marker is indicative of pancreatic cancer or the susceptibility to pancreatic cancer. 2 2

obtaining a compound which interacts with a polypeptide listed in table 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of contacting said polypeptide with a compound or a plurality of compounds under conditions which allow interaction of said compound with said polypeptide; and detecting the interaction The present invention also provides a screening method for identifying and/or between said compound or plurality of compounds with said polypeptide.

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conventional methods. The type of conventional method for testing the interaction of a The "interaction" in the screening methods as disclosed herein may be measured by

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purified from cells that endogenously express the polypeptide. As a non-limiting an in vitro method using either purified recombinant polypeptide, or native polypeptide or other surfaces, and interaction of a compound with the polypeptide can be measured example, a polypeptide of the invention can be bound to beads or immobilized on plastic by either using a labelled compound and measuring the label bound to the polypeptide compound with a polypeptide that is soluble, as opposed to membrane associated, can be

or by displacement of a labeled known ligand from said polypeptide.

interaction of a compound with said polypeptides can be detected with different methods the polypeptide or in which the polypeptide is overexpressed, eg. by detecting For polypeptides that are associated with the cell membrane on the cell surface, or which are expressed as transmembrane or integral membrane polypeptides, the which include, but are not limited to, methods using cells that either normally express displacement of a known ligand which is labeled by the compound to be screened. 2

Alternatively, membrane perparations may be used to test for interaction of a compound with such a polypeptide 12

assays like "Amplified Luminescent Proximity Homogenous AssayTM" (BioSignal Packard) may be employed. Further methods are well known in the art and, inter alia, Interaction assays to be employed in the method disclosed herein may comprise 7405), TR-FRETs and biochemical assays as disclosed herein. Furthermore, commercial PRET-assays (fluorescence resonance energy transfer; as described, inter alia, in Ng. Science 283 (1999), 2085-2089 or Ubarretxena-Belandia, Biochem. 38 (1999), 7398described in Fernandez, Curr. Opin. Chem. Biol. 2 (1998), 547-603.

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hybrid screenings (as, described, inter alia, in EP-0 963 376, WO 98/25947, WO precipitation assays from cell extracts as described, inter alia, in Kasus-Jacobi, Oncogene 19 (2000), 2052-2059, "interaction-trap" systems (as described, inter alia, in US biochemical assays which are well known in the art and which comprise, e.g., homogenous and heterogenous assays as described herein below. Said interaction assays employing read-out systems are well known in the art and comprise, inter alia, two-00/02911; and as exemplified in the appended examples), GST-pull-down columns, co-The "test for interaction" may also be carried out by specific immunological and/or ೪

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6,004,746) expression cloning (e.g. lamda gt11), phage display (as described, inter alia, in US 5,541,109), in vitro binding assays and the like. Further interaction assay methods and WO 00/17221, WO 00/14271 or WO 00/05410. Vidal and Legrain (1999) in Nucleic corresponding read out systems are, inter alia, described in US 5,525,490, WO 99/51741, Acids Research 27, 919-929 describe, review and summarize further interaction assays known in the art which may be employed in accordance with the present invention.

Homogeneous (interaction) assays comprise assays wherein the binding Immuno Radiometric Assays (IRMA), Flow Injection Analysis (FIA), Flow Activated Cell partners remain in solution and comprise assays, like agglutination assays. Heterogeneous assays comprise assays like, inter alia, immuno assays, for example, Enzyme Linked Immunosorbent Assays (ELISA), Radioactive Immunoassays (RIA), Sorting (FACS), Chemiluminescent Immuno Assays (CLIA) or Electrogenerated Chemiluminescent (ECL) reporting.

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has not been contacted with said compound; and d) quantitatively relating the activity as to (c) is indicative for an inhibitor or antagonist. The terms inhibitors and antagonists as used herein are used interchangeably. This screening assay can be performed either as an host may therefore be genetically modified with a nucleic acid molecule encoding such a obtaining a compound which is an inhibitor or an antagonist of a polypeptide listed in able 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of a) contacting said polypeptide with a compound identified and/or obtained by compound with said polypeptide; b) determining the activity of said polypeptide; c) determining the activity of said polypeptide expressed in the host as defined in (a), which determined in (b) and (c), wherein a decreased activity determined in (b) in comparison in vitro assay, or as a host-based assay. The host to be employed in the screening methods of the present invention and comprising and/or expressing a polypeptide listed in table 2, 3, 5 and/or 6 may comprise prokaryotic as well as eukaryotic cells. Said cells may comprise bacterial cells, yeast cells, as well as cultured (tissue) cell lines, inter alia, derived from mammals. Furthermore animals may also be employed as hosts, for example an non-human transgenic animal. Accordingly, said host (cell) may be transfected or transformed with the vector comprising a nucleic acid molecule coding for a polypeptide which is differentially regulated in pancreatic cancer as disclosed herein. Said host cell or The present invention further provides a screening method for identifying and/or the screening method described above under conditions which allow interaction of said 8

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into the host (cell) or into one of its predecessors/parents. The nucleic acid molecule or vector may be present in the genetically modified host cell or host either as an independent molecule outside the genome, preferably as a molecule which is capable of polypeptide or with a vector comprising such a nucleic acid molecule. The term genetically modified" means that the host cell or host comprises in addition to its natural genome a nucleic acid molecule or vector coding for a polypeptide listed in table 2, 3, 5 and/or 6 or at least a fragment therof. Said additional genetic material may be introduced eplication, or it may be stably integrated into the genome of the host cell or host.

cloning like E. coli or Bacillus subtilis. Yet, these prokaryotic host cells are also envisaged example, fungal or animal cells. Examples for suitable fungal cells are yeast cells, As mentioned herein above, the host cell of the present invention may be any prokaryotic or eukaryotic cell. Suitable prokaryotic cells are those generally used for in the screening methods disclosed herein. Furthermore, eukaryotic cells comprise, for preferably those of the genus Saccharomyces and most preferably those of the species Saccharomyces cerevisiae. Suitable animal cells are, for instance, insect cells, vertebrate cells, preferably mammalian cells, such as e.g. CHO, HeLa, NIH3T3 or MOLT-4. Further suitable cell lines known in the art are obtainable from cell line depositories, like the American Type Culture Collection (ATCC). 2

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The hosts may also be selected from non-human mammals, most preferably mice, rats, sheep, calves, dogs, monkeys or apes. As described herein above, said animals/mammals also comprise non-human transgenic animals, which preferably express at least one polypeptide differentially regulated in pancreatic cancer as disclosed herein. Preferably, said polypeptide is a polypeptide which is up-regulated in tissue derived from patients with pancreatic cancer. Yet it is also envisaged that non-human present invention or alternatively, which comprise silenced or less efficient versions of transgenic animals be produced which do not express marker genes as disclosed herein or who express limited amounts of said marker gene products. Said animals are preferably human animals comprising and/or expressing the up-regulated polypeptides of the down-regulated polypeptides are useful models for studying the development of pancreatic cancer and provide for useful models for testing drugs and therapeutics for related to polypeptides which are down-regulated in pancreatic cancer. Transgenic nonpancreatic cancer treatment and/or prevention.

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A compound which interacts with a polypeptide listed in table 2, 3, 5 and/or 6 and which inhibits or antagonizes said polypeptide is identified by determining the activity of said polypeptide in the presence of said compound.

- The term "activity" as used herein relates to the functional property or properties of a specific polypeptide. For the enzymes listed in table 2, 3, 5 and/or 6, the term "activity" relates to the enzymatic activity of a specific polypeptide. Activity assays for the enzymes listed in table 2, 3, 5 and/or 6 are well known.
- not limited to, adhesion assays, cell spreading assays, or in vitro interaction of the For adhesion molecules listed in table 2, 3, 5 and/or 6, the term "activity" relates to the adhesive properties of a polypeptide and may determined using assays such as, but adhesion molecule with a known ligand. Such assays are well known in the art. 유
- staining actin filaments with fluorescently labeled phalloidin. All of these assays are well non-limiting example, the ability of Gelsolin to regulate actin polymerization, or of cell migration assays, cell proliferation assays or immunofluorecence assays, or by For cytoskeletal proteins, the term "activity" relates to the regulation of the cytoskeleton by such polypeptides, or to their incorporation into the cytoskeleton. As a Filamin A to promote orthogonal branching of actin filaments, may be determined using in vitro actin polymerization assays. Activity in relation to the regulation of cytoskeletal structures may further be determined by, as non-limiting examples, cell spreading assays, known to the person skilled in the art. 12 20
- For ion channels (Chloride intracellular channel protein) the term "activity" relates to ion flux (Chloride lux) across the membrane. Methods to determine ion flux across membranes are well known to the person skilled in the art. 52

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For transcription factors, eg. KIAA 1034, the term "activity" relates to their ability to regulate gene transcription. The transcriptional activity of a polypeptide can be determined using commonly used assays, such as a reporter gene assay.

ability to mediate the cellular function or functions eventually caused by growth factor or be determined by testing for receptor auto-phosphorylation, or by assaying for modification or recruitment of downstream signaling mediators to the receptors (by immunoprecipitation and Western Blotting of signaling complexes). Cellular functions regulated by growth factors or hormones and their receptors can be cell proliferation (eg determined by using thymidine incorporation or cell counts), cell migration assays (eg determined by using modified Boyden chambers), cell survival or apoptosis assays (eg determined by using DAPI staining), angiogenesis assays (eg in vitro assays to measure endothelial tube formation that are commercially available). In addition to these assays, activation and subsequent signaling cascades, and/or it relates to the factor's or receptor's hormone mediated receptor activation. Growth factor or hormone binding to receptors can be determined by commonly known ligand binding assays. Receptor activation can For growth factors and hormones or their receptors, the term "activity" relates to their ablitiy to bind to their receptors or ligands, respectively, and to induce receptor other assays may be used as well to determine these and other cellular functions.

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Further to the screening methods disclosed above, this invention provides a screening method for identifying and/or obtaining a compound which is an inhibitor of polypeptide with a compound; b) determining the expression level and/or activity of said polypeptide; c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and d) Inhibitors or antagonists of a polypeptide listed in tables 2 and/or 3 are identified by the screening method described above when there is a decreased activity determined in the presence of the compound in comparison to the absence of the compound in the the expression of a polypeptide listed in tables 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of a) contacting a host which expresses said quantitatively relating the expression level of said polypeptide as determined in (b) and screening method, which is indicative for an inhibitor or antagonist. ಜ

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(c), wherein a decreased expression level determined in (b) in comparison to (c) indicative for an inhibitor of the expression of said polypeptide.

An inhibitor of the expression of a polypeptide listed in table 2, 3, 5 and/or 6 of the protein is determined in the presence of the compound in comparison to the absence of the compound in the screening method, which is indicative for an inhibitor of is identified by the screening method described hereinbefore when a decreased expression expression of a polypeptide.

listed table 2, 3, 5 and/or 6 which is up-regulated in pancreatic cancer, in cells, preferably expression levels of the same polypeptide in healthy pancreatic cells. Preferably, The term "express" as used herein relates to expression levels of a polypeptide in a pancreatic adenocarcinoma cell line, which are elevated as compared to the expression levels are at least 2 fold, more preferably at least 3 fold, even more preferably at least 4 fold, most preferably at least 5 fold higher than in healthy pancreatic cells. 12 2

material can be utilized. The carrier material can be an organic or inorganic one suitable obtained by any of the screening methods hereinbefore described. Said compound is further comprised in a pharmaceutical composition. A method for the preparation of pharmaceutically acceptable carrier or diluent is also claimed. Any conventional carrier gelatin, gum arabic, lactose, starch, magnesium stearate, talc, vegetable oils, polyalkyleneglycols, petroleum jelly and the like. Furthermore, the pharmaceutical preparations may contain other pharmaceutically active agents. Additional additives such as flavoring agents, stabilizers, emulsifying agents, buffers and the like may be added in accordance Furthermore, the present invention provides a compound identified and/or for eteral, percutaneous or parenteral administration. Suitable carriers include water, said pharmaceutical composition comprising formulating said compound in a with accepted practices of pharmaceutical compounding.

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used for the preparation of a diagnostic composition for diagnosing pancreatic cancer or a predisposition for pancreatic cancer.. Preferably, said compound comprises an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense Said compound may be used for the preparation of a medicament for the treatment or prevention of pancreatic cancer. In addition, said compound may also be

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listed in tables 2 and/or 3, or antigen-binding fragments thereof, may be used in an in Within the scope of the present invention, antibodies against the proteins vitro method for the diagnosis of pancreatic cancer.

by this invention is a kit for the diagnosis of pancreatic cancer comprising one or more of by this invention is a kit for screening of compounds that antagonize any of the polypeptides listed in tables 2 and/or 3 or inhibit the expression of any of said provides a kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, described above. Another kit provided the nucleic acids coding for the marker hereinbefore described. Yet another kit provided In order to efficiently perform diagnostic screenings, the present invention 2

The present invention pertains to a marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 6. Preferably, said marker does not include Seq ID No.s 25 and 50 to 55. In a more preferred embodiment, said marker comprises at least one of the polypeptides listed in table 5.

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The present invention also provides an in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of

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a) obtaining a biological sample; and

b) detecting and/or measuring the increase of at least one of the polypeptides listed in table 6.

measuring the decrease of at least one of the polypeptides listed in table 5. More preferably, in said vitro method, said at least one polypeptide does not include Seq ID No.s 25 and 50 to 55. Even more preferably, in said vitro method, said biological sample is derived from the group consisting of serum, plasma, pancreatic juice and cells of Preferably, said in vitro method additionally comprises the step of detecting and/or pancreatic tissue.

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The present invention further provides an in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of

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a) obtaining a biological sample; and

 b) detecting and/or measuring the increase of at least one nucleic acid coding for the marker hereinbefore described. Preferably, in said in vitro method, said nucleic acid molecule is RNA or DNA. More preferably, in said in vitro method, said DNA is a cDNA.

In a further more preferred embodiment of any of the in vitro methods hereinbefore described, the expression levels of at least one of said nucleic acids in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same nucleic acids in a healthy individual. In a most preferred embodiment of any of the in vitro methods hereinbefore described, the expression level of said marker in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same marker in a healthy individual.

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In a further preferred embodiment of the in vitro method hereinbefore described,

an increase of the expression levels of said marker is indicative of pancreatic cancer or the

susceptibility to pancreatic cancer.

The present invention also pertains to a screening method for identifying and/or obtaining a compound which interacts with a polypeptide selected from the group consisting of the polypeptides listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of

- a) contacting said polypeptide with a compound or a plurality of compounds under conditions which allow interaction of said compound with said polypeptide; and
- b) detecting the interaction between said compound or plurality of compounds with said polypeptide.

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Furthermore, the present invention provides a screening method for identifying and/or obtaining a compound which is an inhibitor or an antagonist of a polypeptide listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of

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contacting said polypeptide with a compound identified and/or obtained by
the screening method of claim 39 under conditions which allow interaction of
said compound with said polypeptide;

) determining the activity of said polypeptide;

c) determining the activity of said polypeptide expressed in the host as defined in
 (a), which has not been contacted with said compound; and

d) quantitatively relating the activity as determined in (b) and (c), wherein a decreased activity determined in (b) in comparison to (c) is indicative for an inhibitor or antagonist.

The present invention also provides a screening method for identifying and/or obtaining a compound which is an inhibitor of the expression of a polypeptide selected from the group consisting of the polypeptides listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of

a) contacting a host which expresses said polypeptide with a compound,

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b) determining the expression level and/or activity of said polypeptide;

c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and

d) quantitatively relating the expression level of said polypeptide as determined in (b) and (c), wherein a decreased expression level determined in (b) in comparison to (c) is indicative for an inhibitor of the expression of said polypeptide.

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The present invention provides a compound identified and/or obtained by the screening methods hereinbefore described.

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In addition, the present invention provides a pharmaceutical composition comprising the compound hereinbefore described. Also provided is a method for the preparation of the pharmaceutical composition hereinbefore described comprising to formulating the compound hereinbefore described in a pharmaceutically acceptable carrier or dilutent.

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The present invention provides a use of a compound hereinbefore described for the preparation of a medicament for the treatment or prevention of pancreatic cancer. Also provided is a use of a compound hereinbefore described for the preparation of a diagnostic composition for diagnostic pancreatic cancer or a predisposition for pancreatic cancer. In a preferred embodiment, the uses hereinbefore described relate to a compound comprising an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense construct.

Within the scope of the present invention, antibodies against the proteins
10 listed in tables 5 and/or 6, or antigen-binding fragments thereof, may be used in an in vitro method for the diagnosis of pancreatic cancer.

In order to efficiently perform diagnostic screenings, the present invention provides a kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, described above. Another kit provided by this invention is a kit for the diagnosis of pancreatic cancer comprising one or more of the nucleic acids coding for the marker hereinbefore described. Yet another kit provided by this invention is a kit for screening of compounds that antagonize any of the polypeptides listed in tables 5 and/or 6 or inhibit the expression of any of said polypeptides.

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In the present invention, the proteins, compounds, kits, methods and uses substantially as herein before described, especially with reference to the foregoing examples are also claimed.

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Examples:

Collection of tissue samples

Pancreatic carcinomas and adjacent tissue were collected from the patients listed in

Samples were collected shortly after the resection (less than 30 minutes), and fast frozen in liquid nitrogen for about 1 minute, then stored in a freezer at a temperature of -80°C.

10 Characterization of formalin-fixed specimens

Histopathological characterization was carried out by using hematoxylin-eosin-stained sections of formalin-fixed and paraffin-embedded specimens. Tumors were classified using the WHO system. The types of pancreatic carcinomas included in the study are shown in table 1.

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The twelve pancreatic carcinoma samples used in this study were ductal carcinomas which constitute the overwhelming proportion of pancreatic carcinomas. The patient-matched samples from histologically normal tissue surrounding the carcinoma were used as controls. We carried out 12 pairs of 2-dimensional electrophoresis maps for

- comparing protein expression between tumor tissue and normal control tissue. For protein identification, the samples were pooled, thus generating pan-Carcinoma and pan-Normal protein extracts. Quantification was carried out in two steps: (I) Gels from the pooled samples were compared using the PDQuest image analysis software. (II) The changes identified at the level of the pooled samples were cross-validated by an analysis of
 - 25 the individual samples. The change factors shown in table 2, 3, 5 and 6 were determined using the pooled samples.

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Preparation of samples for electrophoresis

Samples cleaned of clots and contaminating tissue were frozen in liquid nitrogen, then ground to powder. Samples were suspended in lysis buffer (8M urea, 4% CHAPS, 40mMol/L Tris-Cl, 0.5% carier amphollytes, 100mMol/L DTT and 0.1ig/il PMSF) and centrifuged at 12000rpm for 30 minutes. The supernatants were stored at -80°C. The protein concentration in the extracts was determined by the Bradford method (Bradford, M. Anal. Biochem. 72, 248 (1976).

Two-dimensional gel electrophoresis

Samples containing 1 mg of protein were loaded onto the rehydrated IPG strip (18 cm, pH3~10) by using the cup loading method. IEF was performed using Pharmacia Multiphor apparatuses under the following conditions: First, the voltage was increased 200V-5000V over 24hrs, then a constant voltage of 5000V was applied for 24 hrs, the running temperature was 20°C. After IEF, the strips were equilibrated with 10 ml equilibration solution I (6 M Urea, 50 mM Tris pH 8.8, 30 % Glycerol, 2.0 % SDS, 30 mM Dithioerythritol) for 15 min, then for another 15 min with equilibration solution II (6 M Urea, 50 mM Tris pH 8.8, 30 % Glycerol, 2.0 % SDS, 0.23 M Iodoacetamide).

The second dimension SDS polyacrylamide gel electrophoresis (SDS-PAGE) was
carried out using a Hoefer ISO_DALT apparatus (10 gels/run, 24×20 cm), IEF strips were
loaded onto 12% homogeneous polyacrylamide gels (1.5 mm x 24 cm × 20 cm). The gels
were run in TGS_Buffer (250 mM Tris, 1.92 M Glycine, 1% (w/v) SDS, pH = 8.3, BioRad) at a constant voltage (80 V, 20°C).

25 Gel fixation and staining

Gels were fixed in 50% Methanol/20% acetic acid for 30 min, then washed in ultrapure water for 30 min and stained with NOVEX Colloidal Blue staining Kit (Invitrogen) following the manufacturer's recommendations.

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Protein Identification

The protein identification was performed using a two-step procedure.

In-gel digestion

Spots were picked and transferred into 96-well by a spot picking robot. From each gel, 600-800 spots were picked. The spots were destained with 100µl of 30% acentonitrile in 50Mm ammonium bicarbonate, washed in ultra pure-water and dried in a speed vac evaporator. The dry gel pieces were digested with 10ng/µl trypsin (Promega, Madison, USA) solution in 500 nM ammonium bicarbonate at room temperature for 16 h maximum. The peptides from each spot were extracted with 20µl of 0.1% trifluore acetic acid (TFA) in 50% acetonitrile. The matrix solution consisted of 0.025%(w/v) alfacyano-4-hydroxy cinammic acid (Sigma) in 50% acetonitrile(0.1% TFA with internal standard peptides des-Arg-Bradykinin(Sigma, MW 904.4681 Da) and adrenocorticotropic hormone fragment 18-39 (Sigma, MW 2465.1989 Da).

Analysis by MALDI-TOP

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1.5ul of peptide extract and 1.0µl of matrix solution were stimulaneously applied to the spots on the MS target. Recrytallization was carried out as specified by the instruments manufacturer. The samples were analyzed in a MALDI-time of flight Mass spectrometer (Autoflex, Bruker Analytics, Bremen; Germany). Peak annotation and database search by peptide matching was performed by in house developed software. The peptide mass was compared with theoretic peptide masses of all available proteins from all species. The monoisotopic mass was used and a mass tolerence of 0.00259 was allowed. 4 matching peptides were the minimal requirement for an identity assignment. Mismatch or miscleavage sites were not considered.

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- 24 -	opathological characteristics of samples
-	Table 1: Clinical and hist

No. of Samples	Sex	Age	Tumor location	Histology	Metastasis in lymph nodes
PC-01	Male	48	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes
PC-02	Male	89	Head of pancreas	Poorly differentiated adenocarcinoma	Yes
PC-03	Male	44	Head of pancreas	Poorly differentiated ductal adenocarinoma, clear cell type	Yes
PC-04	Male	99	Head of pancreas	Well differentiated ductal adenocarcinoma	Yes
PC-05	Female	45,	Head of pancreas	Well differentiated ductal adenocarcinoma	Š
PC-06	Female	92	Head of pancreas	Well differentiated ductal adenocarcinoma	Yes
C-07	Male	59	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes
80-02	Female	62	Body of pancreas	Well differentiated ductal adenocarcinoma	Yes
60-02	Male	. 54	Head of pancreas	Middle differentiated ductal adenocarcinoma	% 9
C-10	Pemale	53	Head of pancreas	Well differentiated ductal adenocarcinoma	No O
C-11	Female	54	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes
C-12	Female	69	Head of pancreas	Middle differentiated ductal adenocarcinoma	Yes

Table 2: Proteins up-regulated in pancreatic cancer I

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	Protein	Acc No	Description	Seq ID No.	Pold
	sw:CATD_HUMAN	P07339	Cathepsin D precursor (ec 3.4.23.5).		Q
	ew:IDHC_HUMAN	075874	Isocitrate dehydrogenase [NADP] cytoplasmic (ec 1.1.1.1.2)	2	
	sw:GELS_HUMAN	P06396	Gelsolin precursor, plasma	3	
	***CFAB_HUMAN	P00751	Complement factor B precursor (ec 3.4.21.47)	4	8
	SW.AAC4_HUMAN	043707	Alpha-actinin 4 (non-muscle alpha-actinin 4)	2	7
	8W.AAC1_HUMAN	P12814	Alpha-actinin I (alpha-actinin cytoakeletal isoform)	7	7
	sw:TBA4_HUMAN	P05215	Tubulin alpha-4 chain.	&	2
	5w.ABP2_HUMAN	P21333	Filamin A (Endothelial actin-binding protein)	6	4
	sw:TAGL_HUMAN	P37802	Transgelin 2 (smooth muscle protein 22-alpha)	10	2
	sw:TPM4_HUMAN	P07226	Tropomyosin alpha 4 chain	= .	٥
·	6w;BGH3_HUMAN	Q15582	Transforming growth factor-bets induced protein IG-H3 precursor	9	'n
	8w:CALD_HUMAN	Q05682	Caldesmon (cdm)	12	7
	sw:ENOL_HUMAN	Q05524	Alpha enolase	13	7
	sw.ACY1_HUMAN	Q03154	Aminoacylase-1	14	r,
-	sw:CAPB_HUMAN	P47756	P-actin capping protein beta subunit (capz beta)	15	r.
	sw.IPYR_HUMAN	Q15181	Inorganic pyrophosphatase	91	۵
	sw.LEG3_HUMAN	P17931	Galectin-3 (galactose-specific lectin 3).	17.	2

sw:POR2_HUMAN	P45880	Voltage-dependent anion-selective channel protein 2	18	4	
SW:ANX2_HUMAN	P07355	Annezin II	19	7	
ew:CBP2_HUMAN	P50454	Collagen-binding protein 2 precursor	20	2	
sw:COF1_HUMAN	P23528	Cofilin, non-muscle isoform	21	4	
sw:CYPH_HUMAN	P05092	Peptidyl-prolyl cis-trans isomerase A	22	4	
sw:DY12_HUMAN	Q13409	Dynein intermediate chain 2, cytosolic	23	2	
**ECH1_HUMAN	Q13011	Delta3,5-Delta2,4-dienoyl-coa isomerase, mitochondrial precursor	24	2	
sw.MLRN_HUMAN	P24844	Myosin regulatory light chain 2	8	7	
sw.PLSL_HUMAN	P13796	L-Plastin	26	۵	
sw:RAN_HUMAN	P17080	GTP-binding nuclear protein ran	27	m	
sw:ROK_HUMAN	Q07244	Heterogeneous nuclear ribonucleoprotein k	28	7.	
sw:TCTP_HUMAN	P13693	Translationally controlled tumor	29	å	
sw:TPM1_HUMAN	P09493	Tropomyosin I alpha chain	8	۵	
sw:TYPH_HUMAN	P19971	Thymidine phosphorylase precursor	31	s.	
sw.AMPL_HUMAN	P28838	Cytosol aminopeptidase	32	6	
8w:K1CS_HUMAN	P08727	Keratin, type i cytoskeletal 19 (cytokeratin 19)	33	4	
8W:ALDX_HUMAN	P14550	Alcohol dehydrogenase [NADP+]	*	4	
sw:EL3A_HUMAN	P09093	Elastase Illa precursor	35	4	
sw:DLDH_HUMAN	P09622	Dihydrolipoamide dehydrogenase, mitochondrial precursor	%	2	
sw.ECHM_HUMAN	P30084	Enoyl-CoA hydratase, mitochondrial precursor	37	3	
sw:HSBX_HUMAN	014558	Heat-shock 20 kDa like-protein p20.	88	2	

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8W:MLEN_HUMAN	P16475	Myosin light chain alkali, non-muscle isoform	38	6
8W:CALX_HUMAN	P27824	Calnexin precursor	6	6
sw:MA32_HUMAN	Q07021	Complement component 1	4	۵
8w:NUAM_HUMAN	P28331	NADH-ubiquinone oxidoreductase 75 kda subunit, mitochondrial precursor	42	74.
EW:PBEP_HUMAN	P43490	Pre-B cell enhancing factor precursor.	43	2
sw.RET1_HUMAN	P09455	Retinol-binding protein I, cellular	4	2
sw.TCPG_HUMAN	P49368	T-complex protein 1, gamma subunit	45	7
sw:RINI_HUMAN	P13489	Placental ribonuclease inhibitor	46	4
Sw:GBLP_HUMAN	P25388	Guanine nucleotide-binding protein beta subunit-like protein 12,3	47	7
FW:S109_HUMAN	P06702	Calgranulin B	6\$	4

Table 3: Proteins up-regulated in pancreatic cancer II

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Table 4. Proteins roughly classified by their involved biological processing or basic function

Protein	Acc No	Description	Seq ID No	Pold Change
8w:CAPG_HUMAN	P40121	Macrophage capping protein	20	ej.
***ANX1_HUMAN	P04083	Annexin I (lipocortin I) (calpactin II)	51	4
8w:K2C7_HUMAN	P08729	Keratin, type II cytoskeletal 7	52	ĸ
humangp:CHR13- Q15063	Q15063	Osteoblast specific factor 2 precursor	53	2
*w:TGLC_HUMAN	P21980	Protein-glutamine gamma-glutamyltransferase	54	7
8w:GDIR_HUMAN	P52565	Rho GDP-dissociation inhibitor 1	55	. 4
8w:IQG1_HUMAN	P46940	Ras GTPase-activating-like protein	25	2

Protein function	Number ^b	Percentage (%) ^C
Structural constitural and regulation of cytoskeleton	19	20.8
Cell cycle and metabolism	74	25.3
Response to external stimulus or stress	19	20.8
Signal transduction	Ef	77
Nuclear function	18	6.1
Transport processing	19	6.5
Hemostatis	12	1.4
Cell adhension	7	2.4
Chaperon	7	2.4
Apoptosis	3	-
Unknown function	.11	3.7
Others		2.4
Total	293	. 100

Table 5. Proteins with higher levels in normal pancreatic compared to

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8w:PDX4_HUMAN	Q13162	peroxiredoxin 4	2	86
sw:ULA4_HUMAN	P30039	mawd binding protein	a	87
etabolism of biological process				
sw.AMYC_HUMAN	P19961	alpha-amylase 2b precursor	6	88
sw.AMYP_HUMAN	P04746	alpha-amylase, pancreatic precursor	Uncalç ulated	68
sw:ATPA_HUMAN	P25705	atp synthase alpha chain, mitochondrial precursor	٥.	8
sw:BAL_HUMAN	P19835	bile-salt-activated lipase precursor	m	16
sw:LIP1_HUMAN	P54315	pancreatic lipase related protein 1 precursor.	Q	92
swill? HUMAN	P54317	pancreatic lipase related protein 2 precursor	Uncalc ulated	68
sw:LIPP_HUMAN	P16233	triacylglycerol lipase, pancreatic precursor	Uncalc ulated	94
sw.DPY2_HUMAN	Q16555	dihydropyrimidinase related protein-2		
5W:GABT_HUMAN	P80404	4-aminobutyrate aminotransferase	2	96
sw:GATM_HUMAN	P50440	glycine amidinotransferase, mitochondrial precursor	Uncalç	64
sw:GR78_HUMAN	P11021	78 kda gucose-regulated protein precursor (grp 78)	ກ .	86
sw:IP32_HUMAN	Q13347	eukaryotic translation initiation factor 3 subunit 2	7	66
sw.DPY2_HUMAN	Q16555	dihydropyrimidinase related protein-2		100
sw:PGMU_HUMAN	P36871	phosphoglucomutase	2	101
sw:PSA1_HUMAN	P25786	proteasome subunit alpha type 1	2	102
eat shock protein				
fw:HS27_HUMAN	P04792	heat shock 27 kda protein	Uncalc ulated	103
ignaling				
SW:PD61	Q8WUM4	programmed cell death 6 interacting protein	ın	104
nuscle development				

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Uncalç ulated 4 5 a four and a half lim domains 3 Skeletal muscle LIM-protein 2 (SLIM 2)(Four and a half LIM domains protein 3)(FHL.3). collagen alpha 1(vi) chain precursor. pancreatitis-associated protein 1 precursor. lumican precursor cytochrome b5. Q9bva2 Q06141 Q13643 P00167 P12109 P51884 transport of biological process SW:CA16_HUMAN sw.CYB5_HUMAN SW:LUM_HUMAN hsugp:057687-10-0 sw:PAP1_HUMAN SW:sli2 cell adhesion

8

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109

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Table 6 Proteins with higher levels in pancreatic cancer compared to in normal tissue

- 33 -

ewcAcc_HUMAN 014926 fascin 2 (retinal fascin). 2 56 ewcAcc_HUMAN P12814 apha-actinin 1 2 7 ewcAcc_HUMAN P21393 (apha-actinin 4 2 5 ewcAcc_HUMAN P21393 (apha-filamin). 2 19 ewcAND2_HUMAN P07355 human annechi i (lipocortin ii) 2 19 ewcAND2_HUMAN P07355 human annechi i (lipocortin ii) 2 19 ewcCAPB_HUMAN P40121 macrophage capping protein 3 50 ewcDel_HUMAN P182326 chacin capping protein beta 5 15 ewcDel_HUMAN P182329 chacin intermediate chain 2 2 ewcDel_HUMAN P182326 destrin (actin -depolymerizing 2 2 ewcDel_HUMAN P08327 keratin, type ii cytoskeletal 19 4 33 ewcADYLLHUMAN P18796 gelsolin precursor 2 2 2 ewcALLEL_HUMAN P18796 P18796 protein 1) 3 3	Protein *	AccNo	Description	Fold	Seq 1D No.
014926 fasch 2 (retinal fascin). 2	cytoskeletal regulation				:
P12814 alpha-actinin 1	swPSC2_HUMAN	014926	fascin 2 (retinal fascin).	2	26
P21333	FW:AAC1_HUMAN	P12814	alpha-actinin i	2	7
P21333 endothelial actin-binding protein 4	sw:AAC4_HUMAN	043707	alpha-actinin 4	7	5
P07355 human annezin ii (ilpocortin ii) 2	sw.ABP2_HUMAN	P21333	endothelial actin-binding protein (alpha-filamin).	4	6.
Q05682 caldesmon (cdm), 2	6W.ANX2_HUMAN	P07355	human annexin ii (Ilpocortin ii)	2	. 61
P47756 Factin capping protein beta 5	sw:CALD_HUMAN	Q05682	caldesmon (cdm),	7	12
P40121 macrophage capping protein 3 P23528 Cofilin, non-muscle isoform (p18).	sw:CAPB_HUMAN	P47756	f-actin capping protein beta subunit	2	15
P23528 cofilin, non-muscle isoform (p18).	sw:CAPG_HUMAN	P40121	macrophage capping protein	6	ક્ક
P18282 Gestrin (actin-depolymerizing factor) (add). Goldon Goldon	sw:COP1_HUMAN	P23528	cofilin, non-muscle isoform (p18).	a	21
Q13409 20fragment). 2 20fragment). 2 20fragment). 2 20fragment). 2 2 2 2 2 2 2 2 2	sw.DEST_HUMAN	P18282	destrin (actin-depolymerizing factor) (adf).	. 2	57
P06396 gelsolin precursor	8w:DY12_HUMAN	Q13409	dynein intermediate chain 2(fragment).	7	23
P08727 keratin, type il cytoakeletal 19 4	SW-GELS_HUMAN	P06396	gelsolin precursor	9	9
P08729 keratin, type ii cytoskeletal 7 5	sw:K1CS_HUMAN	P08727	keratin, type i cytoskeletal 19	4	33
P16475 myosin light chain alkali	sw:K2C7_HUMAN	P08729	keratin, type ii cytoskeletal 7	20	52
P13796 -Plastin (tymphocyte cytosolic -Plastin (tymphocyte cytosolic -2 -2 -2 -2 -2 -2 -2 -	8W:MLEN_HUMAN	P16475	myosin light chain alkali	6	. 39
P37802 transgelin (22 kda secin-binding 2	sw.PLSL_HUMAN	P13796	1-plastin (lymphocyte cytosolic protein 1)	4	56
P05215 tubulin alpha-4 chain. 2	sw:TAGL_HUMAN	P37802	transgelin (22 kda actin-binding protein).	77	2
Q03154 aminoacylase-1 5 P28838 cathepain d precursor. 207339 cathepain d precursor. <2	sw:TBA4_HUMAN	P05215	tubulin alpha-4 chain.	7	80
Q03154 aminoscylase-1 5 P28838 cytosol aminopeptidase 3 P07339 cathepsin d precursor. <2	proteolysis and peptidolysis				
P28838 cytosol aminopeptidase 3 P07339 cathepain d precursor. <2	8w.ACY1_HUMAN	Q03154	aminoacylase-1	5.	14
P07339 cathepsin d precursor.	sw:AMPL_HUMAN	P28838	cytosol aminopeptidase	m	32
	sw:CATD_HUMAN	P07339	cathepsin d precursor.	2	-

w:CPAB_HUMAN	P00751	complement factor b precursor	5	4	
w:BL3A_HUMAN	P09093	elastase ilia precursor	4	35	
haperon					
w.APE_HUMAN	P02649	apolipoprotein e precursor (apo-e).	2	59	
w:CALX_HUMAN	P27824	calnexin precursor(p90)	m	40	
M:CYPH_HUMAN	P05092	peptidyi-prolyi cis-trans isomerase a	a	22	
w:TCPG_HUMAN	P49368	t-complex protein 1, gamma subunit	74	45	
w:CBP2_HUMAN	P50454	human. collagen-binding protein 2 precurso	7	20	
_hum:Q96C61	Q96C61	hypothetical 88.6 kda protein	5	99	
xidoreductase					
w:DLDH_HUMAN	P09622	dihydrolipoamide dehydrogenase	2	36	
widhc_human*	075874	isocitrate dehydrogenase [nadp] cytoplasmic	7	2	
w:NUAM_HUMAN	P28331	nadh-ublquinone oxidoreductase 75 kda subunit	7	42	
netabolism of biological process	seas				
W.ALDX_HUMAN	P14550	alcohol dehydrogenase [nadp+]	4	34	
#BCH1_HUMAN	Q13011	delta3,5-delta2,4-dienoyl-coa isomerase	7	24	
w.ECHM_HUMAN	P30084	enoyl-coa hydratase, mitochondrial precursor	m	37	
MIPYR_HUMAN	Q15181	inorganic pyrophosphatase	4	91	
W.TYPH_HUMAN	P19971	thymidine phosphorylase precursor	S	31	
W:ENOA_HUMAN	P06733	human alpha enolase	2	19	
WENOL_HUMAN	Q05524	alpha enolase, lung specific	7	13	
W:SYW_HUMAN	P23381	tryptophanyl-tma synthetase	7	62	
eat shock protein					
w:HSBX_HUMAN	014558	heat-shock 20 kda like-protein p20.	7	38	
ignaling					
#:GBLP_HUMAN	P25388	guanine nucleotide-binding protein beta subunit-like protein 12.3	7	47	

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 8w:GDIR_HUMAN	P52565	tho gdp-dissociation inhibitor 1	0	55
 swilQG1_HUMAN	P46940	ras gtpase-activating-like protein iqgap l	2	25
 ew:PBEP_HUMAN	P43490	pre-b cell enhancing factor precursor.	2	43
sw:RAN_HUMAN	P17080	gtp-binding nuclear protein ran	9	7.7
 immune response				
sw:KAC_HUMAN	P01834	ig kappa chain c region.	2	63
 8w:MA32_HUMAN	Q07021	pre-mma splicing factor sf2, p32 subunit.	4	4
inflammatory reponse				
sw:ANX1_HUMAN	P04083	annexin i (lipocortin i)	4	15
ew:LEG3_HUMAN	P17931	galectin-3	2	17
8w:S109_HUMAN	P06702	calgranulin b (mrp-14)	7	49
muscle development				
sw.TPM1_HUMAN	P09493	tropomyosin I alpha chain	7	30
sw.TPM4_HUMAN	P07226	tropomyosin alpha 4 chain	4	=
sw:MLRN_HUMAN	P24844	myosin regulatory light chain 2	7	848
 transport of biological process				
humangp:CHR2-Q15092	Q15092	transmembrane protein.	7	99
 sw:POR2_HUMAN	P45880	voltage-dependent anion-selective channel protein 2	å.	18
sw:RET1_HUMAN	P09455	retinol-binding protein I	2.	4
RNA processing				
humangp:CHR20-Q9P2E9	075300	ribosome binding protein 1 (kiaa1398 protein).	Q	65
sw:RINI_HUMAN	P13489	placental ribonuclease inhibitor	å	46
8w:ROK_HUMAN	Q07244	heterogeneous nuclear ribonucleoprotein k	2	28
blood coagulation				
*w.FIBG_HUMAN	P02679	fibrinogen gamma chain precursor	6	8
sw:THRB_HUMAN	P00734	prothrombin precursor	4	29
Anti-apoptosis				

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sw:TCTP HUMAN	P13693	translationally controlled tumor	å	29	
		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			
cell adhesion					
humangp:CHR13-Q15063	Q15063	osteoblast specific factor 2 precursor	7	53	
sw:BGH3_HUMAN	Q15582	transforming growth factor-beta induced protein	ď	9	
other					
sw:TGLC_HUMAN	P21980	P21980 tissue transglutaminase	7	54	
sw.KPY1_HUMAN	P14618	Human pyruvate kinase, cytosolic thyroid hormone-binding protein	6	89	
humangp:CHR19-Q96D15	Q96D15	Q96D15 Reticulocalbin 3 precursor.	2	69	
				-	

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Claims

- A marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in tables 2 and 3.
- 5 2. The marker of claim I wherein the group from which at least one polypeptide is selected consists of the polypeptides listed in table 2.
- A polypeptide selected from the group consisting of the polypeptides listed in tables
 and 3, for use as a marker or as a component of a marker for diagnosis of pancreatic
 cancer and/or the susceptibility to pancreatic cancer.
- 4. An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of
- a) obtaining a biological sample; and
- b) detecting and/or measuring the increase of a marker of claims 1 or 2.
- The in vitro method of claim 4, wherein the marker comprises at least two polypeptides.
- 20 6. The in vitro method of claims 4 or 5 wherein said biological sample is derived from the group consisting of serum, plasma, pancreatic juice and cells of pancreatic tissue.
- An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of
- 25 a) obtaining a biological sample; and
- b) detecting and/or measuring the increase of at least one nucleic acid coding for the marker of claims 1 or 2.

PCT/EP2003/014057 WO 2004/055519 The in vitro method of claim 7, wherein said nucleic acid molecule is RNA or DNA.

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The in vitro method of claim 8, wherein said DNA is a cDNA. 6.

The in vitro method of any one of claims 7 to 9, wherein the expression levels of at least one of said nucleic acids in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same nucleic acids in a healthy individual. . 10

2

11. The in vitro method of any one of claims 4 to 6, wherein the expression level of said susceptible to pancreatic cancer is compared to the expression levels of the same marker marker in an individual suspected to suffer from pancreatic cancer and/or to be in a healthy individual.

12

- The in vitro method of claim 11, wherein an increase of the expression levels of said marker is indicative of pancreatic cancer or the susceptibility to pancreatic cancer. 12.
- A screening method for identifying and/or obtaining a compound which interacts with a polypeptide listed in tables 2 and/or 3 whose expression is upregulated in pancreatic cancer, comprising the steps of 13. 2
- under conditions which allow interaction of said compound with said polypeptide; a) contacting said polypeptide with a compound or a plurality of compounds
- b) detecting the interaction between said compound or plurality of compounds with said polypeptide. 22

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inhibitor or an antagonist of a polypeptide listed in tables 2 and/or 3 whose expression is 14. A screening method for identifying and/or obtaining a compound which is an upregulated in pancreatic cancer, comprising the steps of

- the screening method of claim 13 under conditions which allow interaction of said a) contacting a said polypeptide with a compound identified and/or obtained by compound with said polypeptide;
- b) determining the activity of said polypeptide;
- c) determining the activity of said polypeptide expressed in the host as defined in (a), which has not been contacted with said compound; and
- decreased activity determined in (b) in comparison to (c) is indicative for an d) quantitatively relating the activity as determined in (b) and (c), wherein a inhibitor or antagonist.

ទ

- inhibitor of the expression of a polypeptide listed in tables 2 and/or 3 whose expression is 15. A screening method for identifying and/or obtaining a compound which is an upregulated in pancreatic cancer, comprising the steps of 2
- a) contacting a host which expresses said polypeptide with a compound,
- b) determining the expression level and/or activity of said polypeptide;
- c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and

- d) quantitatively relating the expression level of said polypeptide as determined in
- (b) and (c), wherein a decreased expression level determined in (b) in comparison
 - to (c) is indicative for an inhibitor of the expression of said polypeptide.
- 25 16. A compound identified and/or obtained by the screening methods of any one of claims 13 to 15.
- 17. A pharmaceutical composition comprising the compound of claim 16.

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18. A method for the preparation of the pharmaceutical composition of claim 17 comprising formulating the compound of claim 16 in a pharmaceutically acceptable carrier or diluent.

5 19. Use of a compound of claim 16 for the preparation of a medicament for the treatment or prevention of pancreatic cancer. 20. Use of a compound of claim 16 for the preparation of a diagnostic composition for diagnosing pancreatic cancer or a predisposition for pancreatic cancer.

2

21. The use of claim 19 or 20 wherein said compound comprises an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense construct.

22. Antibodies against the proteins listed in tables 2 and/or 3, or antigen-binding fragments thereof, for the use in an in vitro method for the diagnosis of pancreatic

23. A kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, of claim 22.

20

24. A kit for the diagnosis of pancreatic cancer comprising one or more of the nucleic acids coding for the marker of claims 1 or 2.

25. A kit for screening of compounds that activate or inhibit any of the polypeptides25 listed in tables 2 and/or 3, or stimulate or inhibit the expression of any of said polypeptides.

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26. A marker for diagnosis of pancreatic cancer comprising at least one polypeptide selected from the group consisting of the polypeptides listed in table 6.

The marker of daim 26, wherein said at least one polypeptide does not include Seq
 ID No.s 25 and 50 to 55.

28. The marker according to any one of claims 26 to 27, additionally comprising at least one of the polypeptides listed in table 5.

10 29. An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of

a) obtaining a biological sample; and

b) detecting and/or measuring the increase of at least one of the polypeptides listed in table 6.

15

30. The in vitro method of claim 29, additionally comprising the step of detecting and/or measuring the decrease of at least one of the polypeptides listed in table 5.

31. The in vitro method of claims 29 or 30, wherein said at least one polypeptide does

20 not include Seq ID No.s 25 and 50 to 55.

32. The in vitro method of any one of claims 29 to 31, wherein said biological sample is derived from the group consisting of serum, plasma, pancreatic juice and cells of pancreatic tissue.

22

33. An in vitro method for the diagnosis of pancreatic cancer and/or the susceptibility to pancreatic cancer comprising the steps of

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a) obtaining a biological sample; and

b) detecting and/or measuring the increase of at least one nucleic acid coding for the marker of any one of claims 26 to 28.

- The in vitro method of claim 33, wherein said nucleic acid molecule is RNA or DNA
- 35. The in vitro method of claim 34, wherein said DNA is a cDNA.
- 10 36. The in vitro method of any one of claims 33 to 35, wherein the expression levels of at least one of said nucleic acids in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same nucleic acids in a healthy individual.
- 15 37. The in vitro method of any one of claims 33 to 36, wherein the expression level of said marker in an individual suspected to suffer from pancreatic cancer and/or to be susceptible to pancreatic cancer is compared to the expression levels of the same marker in a healthy individual.
- 20 38. The in vitro method of claim 37, wherein an increase of the expression levels of said marker is indicative of pancreatic cancer or the susceptibility to pancreatic cancer.
- 39. A screening method for identifying and/or obtaining a compound which interacts with a polypeptide selected from the group consisting of the polypeptides listed in table 6
 25 whose expression is upregulated in pancreatic cancer, comprising the steps of
- a) contacting said polypeptide with a compound or a plurality of compounds under conditions which allow interaction of said compound with said polypeptide;

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 b) detecting the interaction between said compound or plurality of compounds with said polypeptide.

- 40. A screening method for identifying and/or obtaining a compound which is an inhibitor or an antagonist of a polymentide listed in table 6 whose expression is
 - inhibitor or an antagonist of a polypeptide listed in table 6 whose expression is upregulated in pancreatic cancer, comprising the steps of
- a) contacting said polypeptide with a compound identified and/or obtained by the screening method of claim 39 under conditions which allow interaction of said compound with said polypeptide;
- b) determining the activity of said polypeptide;
- c) determining the activity of said polypeptide expressed in the host as defined in (a), which has not been contacted with said compound; and
- d) quantitatively relating the activity as determined in (b) and (c), wherein a decreased activity determined in (b) in comparison to (c) is indicative for an inhibitor or antagonist.

- 41. A screening method for identifying and/or obtaining a compound which is an inhibitor of the expression of a polypeptide selected from the group consisting of the polypeptides listed in table 6 whose expression is upregulated in pancreatic cancer,
 - 20 comprising the steps of
- a) contacting a host which expresses said polypeptide with a compound,
- b) determining the expression level and/or activity of said polypeptide;
- c) determining the expression level and/or activity of said polypeptide in the host as defined in (a), which has not been contacted with said compound; and
- d) quantitatively relating the expression level of said polypeptide as determined in (b) and (c), wherein a decreased expression level determined in (b) in comparison to (c) is indicative for an inhibitor of the expression of said polypeptide.

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42. A compound identified and/or obtained by the screening methods of any one of

claims 39 to 41.

43. A pharmaceutical composition comprising the compound of claim 42.

comprising formulating the compound of claim 42 in a pharmaceutically acceptable 44. A method for the preparation of the pharmaceutical composition of claim 43

carrier or diluent.

10 45. Use of a compound of claim 42 for the preparation of a medicament for the

treatment or prevention of pancreatic cancer.

46. Use of a compound of claim 42 for the preparation of a diagnostic composition for diagnosing pancreatic cancer or a predisposition for pancreatic cancer.

2

The use of claim 45 or 46 wherein said compound comprises an antibody, an antibody-derivative, an antibody fragment, a peptide or an antisense construct.

48. Antibodies against the proteins listed in tables 5 and/or 6, or antigen-binding fragments thereof, for the use in an in vitro method for the diagnosis of pancreatic 20

49. A kit for the diagnosis of pancreatic cancer comprising one or more of the antibodies, or antigen-binding fragments thereof, of claim 48.

25

50. A kit for the diagnosis of pancreatic cancer comprising one or more of the nucleic acids coding for the marker of claims 26 to 28.

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51. A kit for screening of compounds that activate or inhibit any of the polypeptides listed in table 5 and/or 6, or stimulate or inhibit the expression of any of said polypeptides.

The kit of claim 51, wherein said polypeptides are the polypeptides listed in table 6.

52.

53. The proteins, compounds, kits, methods and uses substantially as herein before described, especially with reference to the foregoing examples.

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Met Gin Pro Ser Ser Leu Leu Ala Ala Ala Lye Phe Asp Giy Iile Leu Giy Met Ala Tyx Pro Arg Ille Ser 20 1 5 20 195 200 205 20 195 200 205 205 20 20 195 200 205 20 20 20 20 205 20 20 20 20 20 20 20 20 20 20 20 20 21 20 20 20 21 20 21 20 20 21 21 21 22 20 21 20 21 22 20 21 20 21 20 20 21 20 21 20 20 40 45 20 20 20 20 22 20 20 20 20 20 20 20 20			185
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Pro Ale Ser Ale Leu Val Arg Ile Pro Leu His Lys Phe Thr Ser Ile 20 210 210 215 220 Arg Arg Thr Met Ser Glu Val Gly Gly Ser Val Glu Asp Leu Ile Ala 35 40 45 225 230 230 230 230 230 235		. 10 .	195 200
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340 345 350	20 25 30
15 Asp Tyr Thr Leu Lys Val Ser Gln Ala Gly Lys Thr Leu Cys Leu Ser	15 Pro Tyr Val Glu Leu Asp Leu His Ser Tyr Asp Leu Gly Ile Glu Asn
355 360 365	35 40 45
Gly Phe Met Gly Met Asp Ile Pro Pro Ser Gly Pro Leu Trp Ile	Arg Asp Ala Thr Asn Asp Gin Val Thr Lys Asp Ala Ala Glu Ala Ile
370 375 380	
Leu Gly Asp Val Phe Ile Gly Arg Tyr Tyr Thr Val Phe Asp Arg Asp	Lys Lys His Asn Val Gly Val Lys Cys Ala Thr Ile Thr Pro Asp Glu
20 385 390 395 400	20 65 70 75 80
Asn Asn Arg Val Gly Phe Ala Glu Ala Ala Arg Leu	Lys Arg Val Glu Glu Phe Lys Leu Lys Gln Met Trp Lys Ser Pro Asn
405 410	56 06 58

Gly Thr lie Arg Asn Ile Leu Gly Gly Thr Val Phe Arg Glu Ala Ile

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	Ile Cys Lys Asn	ile Cys Lys Asn ile Pro Arg Leu Val Ser Gly Trp Val	ly Trp Val Lys Pro Ile	Ala Glu Ala Ala His Gly Th	Ala Glu Ala Ala His Gly Thr Val Thr Arg His Tyr Arg Met Tyr Gln	
	11.5	120	125	305 310	315 320	
	ile ile Gly Arg	ile ile Gly Arg His Ala Tyr Gly Asp Gln Tyr Arg Ala	yr Arg Ale Thr Asp Phe	Lys Gly Gln Glu Thr Ser Th	Lys Gly Gln Glu Thr Ser Thr Asn Pro 11e Ala Ser 11e Phe Ala Trp	
	130	135	140	325	330 335	
ĸ	Val Val Pro Gly	5 Val Val Pro Gly Pro Gly Lys Val Glu Ile Thr Tyr	hr Tyr Thr Pro Ser Asp	5 Thr Arg Gly Leu Ala His Ar	Thr Arg Gly Leu Ala His Arg Ala Lys Leu Asp Asn Asn Lys Glu Leu	
	145	150 15	155 160	340	345 350	
	Gly Thr Gln Lys	Gly Thr Gln Lys Val Thr Tyr Leu Val His Asn Phe Glu-	sn Phe Glu Glu Gly Gly	Ala Phe Phe Ala Asn Ala Le	Ala Phe Phe Ala Asn Ala Leu Glu Glu Val Ser Ile Glu Thr Ile Glu	
	•	165 170	175		360 365	
	Gly Val Ala Met (Gly Val Ala Met Gly Met Tyr Asn Gln Asp Lys Ser	ys Ser Ile Glu Asp Phe	Ala Gly Phe Met Thr Lys As	Ala Gly Phe Met Thr Lys Asp Leu Ala Ala Cys Ile Lys Gly Leu Pro	
01	180	185	061	10 370 . 375	380	
	Ala His Ser Ser	Ala His Ser Ser Phe Gln Met Ala Leu Ser Lys Gly Trp	/8 Gly Trp Pro Leu Tyr	Asn Val Gln Arg Ser Asp Ty	Asn Val Gln Arg Ser Asp Tyr Leu Asn Thr Phe Glu Phe Met Asp Lys	
	195	200	205	385 . 390	395	
	Leu Ser Thr Lys ;	Leu Ser Thr Lys Asn Thr Ile Leu Lys Lys Tyr Asp Gly Arg Phe Lys	r Asp Gly Arg Phe Lys	Leu Gly Glu Asn Leu Lys Il	Leu Gly Glu Asn Leu Lys Ile Lys Leu Ala Gln Ala Lys Leu	•
	210	215	220	405	410	
15	Asp Ile Phe Gln (Asp lie Phe Gin Glu Ile Tyr Asp Lys Gin Tyr Lys Ser Gin Phe Glu	/r Lys Ser Gin Phe Glu .	15.		
	225	230 235	35 240			
	Ala Gln Lys Ile	Ala Gin Lys Ile Trp Tyr Glu His Arg Leu Ile Asp Asp Met Val Ala	te Asp Asp Met Val Ala	<210> 3		
	.,	245 250		. <211> 782		
	Gln Ala Met Lys	Gln Ala Met Lys Ser Glu Gly Gly Phe Ile Trp Ala Cys Lys Asn Tyr	p Ala Cys Lys Asn Tyr	<212> PRT		
20	260	. 265	270	20 <213> Homo sapiens		
	Asp Gly Asp Val (Asp Gly Asp Val Gln Ser Asp Ser Val Ala Gln Gly Tyr Gly Ser Leu	n Gly Tyr Gly Ser Leu	<220>		
	275	280	285	<221> Gelsolin precursor, plasma	plasma	
	Gly Met Met Thr &	Gly Met Met Thr Ser Val Leu Val Cys Pro Asp Gly Lys Thr Val Glu	p Gly Lys Thr Val Glu	<222> (1)(782)		
	290	295	300	<223> Accession No. as of	Accession No. as of 06 Dec 2002; P06396	

_	WO 2004/055519									
		7/335		FC 1/EF 2003/01403/		≩	WO 2004/055519	:/8	8/335	PCT/EP2003/014057
	<400> 3						Lys His Val Val Pro Asn Glu Val Val Gln Arg Leu Phe Gln Val	Asn Glu Val V	Val Val Gln Arg 1	Leu Phe Gln Val
						•	180	н	185	190
	Met Ala Pro His Arg Pro Ala Pro Ala Leu Leu Cys Ala L	Pro Ala Pro Ala	Leu Leu Cys Ala	ı Leu Ser Leu		H	Lys Gly Arg Arg Val Val Arg Ala Thr Glu Val Fro Val Ser Trp Glu	Val Arg Ala I	rhr Glu Val Pro V	Al Ser Trp Glu
	1 5		10	15	•		195	200		. 205
S	5 Ala Leu Cys Ala Leu Ser Leu Pro Val Arg Ala Ala Thr Ala Ser Arg	Ser Leu Pro Val	Arg Ala Ala Thr	Ala Ser Arg		so	Ser Phe Asn Asn Gly Asp Cys Phe Ile Leu Asp Leu Gly Asn Asn Ile	Asp Cys Phe I	tle Leu Asp Leu G	31y Asn Asn Ile
	20	25		30			210	215	220	
	Gly Ala Ser Gin Ala Gly Ala Pro Gin Gly Arg Val Pro Glu Ala Arg	3ly Ala Pro Gln	Gly Arg Val Pro	Glu Ala Arg		æ	His Gin Try Cys Gly Ser Asn Ser Asn Arg Tyr Glu Arg Leu Lys Ala	Ser Asn Ser A	18n Arg Tyr Glu ?	Arg Leu Lys Ala
	35	40	45			N	225	230	235	240
	Pro Asn Ser Met Val Val Glu His Pro Glu Phe Leu Lys Ala Gly Lys	al Glu His Pro	Glu Phe Leu Lys	Ala Gly.Lys		H	Thr Gln Val Ser Lys Gly 11e Arg Asp Asn Glu Arg Ser Gly Arg Ala	Gly Ile Arg A	18p Asn Glu Arg S	ser Gly Arg Ala
01		55	09			. 10	245		250	255
	Glu Pro Gly Leu Gln Ile Trp Arg Val Glu Lys Phe Asp Leu Val Pro	tle Trp Arg Val	Glu Lys Phe Asp	Leu Val Pro		«	Arg Val His Val Ser Glu Glu Gly Thr Glu Pro Glu Ala Met Leu Gln	Glu Glu Gly T	hr Glu Pro Glu A	ila Met Leu Gln
	65	70	75 ·	08			260		265	270
	Val Pro Thr Asn Leu Tyr Gly Asp Phe Phe Thr Gly Asp Ala Tyr Val	byr Gly Asp Phe	Phe Thr Gly Asp	Ala Tyr Val		> .	Val Leu Gly Pro Lys Pro Ala Leu Pro Ala Gly Thr Glu Asp Thr	Pro Ala Leu P.	TO Ala Gly Thr G	ilu Asp Thr Ala
	85	-	06	95		÷	. 572	280		285
15	ile Leu Lys Thr Val Gin Leu Arg Asn Gly Asn Leu Gin Tyr Asp Leu	iln Leu Arg Asn	Gly Asn Leu Gln	Tyr Asp Leu		15 E	Lys Glu Asp Ala Ala Asn Arg Lys Leu Ala Lys Leu Tyr Lys Val	Asn Arg Lys L	eu Ala Lys Leu T	yr Lyg Val Ser
	100	105		110		. ·	. 067	295	300	
	His Tyr Try Leu Gly Asn Glu Cys Ser Gln Asp Glu Ser Gly Ala Ala	ısın Glu Cya Ser (Gin Asp Glu Ser	Gly Ala Ala		4	Asn Gly Ala Gly Thr Met Ser Val Ser Leu Val Ala Asp Glu Asn Pro	Met Ser Val S	er Leu Val Ala A	sp Glu Asn Pro
	115	120	125			m	305	310	315	320
	Ala Ile Phe Thr Val Gln Leu Asp Asp Tyr Leu Asn Gly Arg Ala Val	ln Leu Asp Asp	Tyr Leu Asn Gly	Arg Ala Val		Δί	Phe Ala Gin Gly Ala Leu Lys Ser Giu Asp Cys Phe ile Leu Asp His	Leu Lys Ser G.	lu Asp Cys Phe I	le Leu Asp His
70	130	135	140			20	325		330	335
	Gln His Arg Glu Val Gln Gly Phe Glu Ser Ala Thr Phe Leu Gly Tyr	ln Gly Phe Glu	Ser Ala Thr Phe	Leu Gly Tyr			Gly Lys Asp Gly Lys Ile Phe Val Trp Lys Gly Lys Gln Ala Asn Thr	Ile Phe Val T:	тр гув Сју гув С	ln Ala Aen Thr
	145	150	155	160			340	ň	345	350
	Phe Lys Ser Gly Leu Lys Tyr Lys Lys Gly Gly Vai Ala Ser Gly Phe	ys Tyr Lys Lys (Gly Gly Vai Ala	Ser Gly Phe		O	Glu Glu Arg Lys Ala Ala Leu Lys Thr Ala Ser Asp Phe Ile Thr Lys	Ala Leu Lys Ti	hr Ala Ser Asp P	he Ile Thr Lys
	165	0	170	175			355	360	, ET	365

	WO 2004/055519 9/335	PCT/EP2003/014057 35	WO 2004/055519 PCT/EP2003/014057
	Met Asp Tyr Pro Lys Gln Thr Gln Val Ser Val Leu	al Ser Val Leu Pro Glu Gly Gly	Ala Ser Thr Arg Leu Phe Gln Val Arg Ala Asn Ser Ala Gly Ala Thr
	370 375	380	. 576 570 575
	Glu Thr Pro Leu Phe Lys Gln Phe Phe Lys Asn Trp	ne Lys Asn Txp Arg Asp Pro Asp	Arg Ala Val Glu Val Leu Pro Lys Ala Gly Ala Leu Asn Ser Asn Asp
	385 390	395	065 585 085
٧n	Gln Thr Asp Gly Leu Gly Leu Ser Tyr Leu Ser Ser His Ile Ala Asn	yr Leu Ser Ser His Ile Ala Asn	5 Ala Phe Val Leu Lys Thr Pro Ser Ala Ala Tyr Leu Trp Val Gly Thr
	405	410 415	265
	Val Glu Arg Val Pro Phe Asp Ala Ala Thr Leu His Thr	la Thr Leu His Thr Ser Thr Ala	Gly Ala Ser Glu Ala Glu Lys Thr Gly Ala Gln Glu Leu Leu Arg Val
	420 42	430	610 615 620
	Met Ala Ala Gln His Gly Met Asp Asp Asp Gly Thr Gly Gln Lys	sp Asp Gly Thr Gly Gln Lys Gln	Leu Arg Ala Gln Pro Val Gln Val Ala Glu Gly Ser Glu Pro Asp Gly
10	435 440		10 · 625 630 635 640
	ile Trp Arg ile Glu Gly Ser Asn Lys Val Pro Val Asp Pro Ala Thr	ys Val Pro Val Asp Pro Ala Thr	Phe Trp Glu Ala Leu Gly Gly Lys Ala Ala Tyr Arg Thr Ser Pro Arg
	450 455	460	645 650 655
	Tyr Gly Gln Phe Tyr Gly Gly Asp Ser Tyr ile Ile	er Tyr Ile Ile Leu Tyr Asn Tyr	Leu Lys Asp Lys Met Asp Ala His Pro Pro Arg Leu. Phe Ala Cys
	465 470	475 480	660 665 670
15	Arg His Gly Gly. Arg Gln Gly Gln Ile Ile Tyr Asn 1	le Ile Tyr Asn Trp Gln Gly Ala	is Ser Asn Lys Ile Gly Arg Phe Val Ile Glu Glu Val Pro Gly Glu Leu
	485	490 495	675 680 685
	Gln Ser Thr Gln Asp Glu Val Ala Ala Ser Ala Ile	la Ser Ala Ile Leu Thr Ala Gln	Met Gin Glu Asp Leu Ala Thr Asp Asp Val Met Leu Leu Asp Thr Trp
	200 200	505 510	690 695 700
	Leu Asp Glu Glu Leu Gly Gly Thr Pro Val Gln Ser	ro Val Gln Ser Arg Val Val Gln	Asp Gln Val Phe Val Trp Val Gly Lys Asp Ser Gln Glu Glu Glu Lys
70	515 520	525	20 705 710 715 720
	Gly Lys Glu Pro Ala His Lau Met Ser Leu Phe Gly	er Leu Phe Gly Gly Lys Pro Met	Thr Glu Ala Leu Thr Ser Ala Lys Arg Tyr Ile Glu Thr Asp Pro Ala
	. 530 535	. 540	725 730 735
	Ile Ile Tyr Lys Gly Gly Thr Ser Arg Glu Gly Gly Gln Thr Ala Pro	rg Glu Gly Gly Gln Thr Ala Pro	Asn Arg Asp Arg Thr Pro Ile Thr Val Val Lys Gln Gly Phe Glu
	545 550		740 . 745 750

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Pro Pro Ser Phe Val Gly Trp Phe Leu Gly Trp Asp Asp Asp Tyr Trp	Gly Phe Tyr Pro Tyr Pro Val Gln Thr Arg Thr Cys Arg Ser Thr Gly
755 760 . 765	65 70 75 80
Ser Val Asp Pro Leu Asp Arg Ala Met Ala Glu Leu Ala Ala	Thr Val Arg Lys
775 780	56 06 58
	5 Glu Cys Arg Ala 11e His Cys Pro Arg Pro His Asp Phe Glu Asn Gly
	100 105 110
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<211> 764	115 120 125
<212> PRT	Phe His Cys Tyr Asp Gly Tyr Thr Leu Arg Gly Ser Ala Asn Arg Thr
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1 5 10 15	195 200 205
Gly Leu Leu Ser Gly Gly Val Thr Thr Pro Trp Ser Leu Ala Arg	Gly Ser Trp Ser Gly Thr Glu Pro Ser Cys Gln Asp Ser Phe Met Tyr
20 25 30	20 210 215 220
Pro Gln Gly Ser Cys Ser Leu Glu Gly Val Glu Ile Lys Gly Gly Ser	Asp Thr Pro Gln Glu Val Ala Glu Ala Phe Leu Ser Leu Thr Glu
35 . 40 45	. 225 . 230 . 235 . 240
Phe Arg Leu Leu Gln Glu Gly Gln Ala Leu Glu Tyr Val Cys Pro Ser	Thr lle Glu Gly Val Asp Ala Glu Asp Gly His Gly Pro Gly Glu Gln
SO 55 60	245 . 250 255

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625 630 635 640	435 440 445
Ala Gln Asp Ile Lys Ala Leu Phe Val Ser Glu Glu Lys Lys Leu	Leu Val Asn Gln Val Asn Ile Asn Ala Leu Ala Ser Lys Lys Asp Asn
610 615 620	420 425 430
Leu Pro Pro Thr Thr Cys Gln Gln Glu Glu Leu Leu Pro	Asn Pro Arg Glu Asp Tyr Leu Asp Val Tyr Val Phe Gly Val Gly Pro
20 595 600 605	20 405 410 415
Arg Pro Ile Cys Leu Pro Cys Thr Glu Gly Thr Thr Arg Ala Leu Arg	Val lle Asp Glu lle Arg Asp Leu Leu Tyr lle Gly Lys Asp Arg Lys
	385 390 395 400
Val Ala Leu Ile Lys Leu Lys Asn Lys Tyr Gly Gln Thr Ile	ile beu Met Thr Asp Gly beu His Asn Met Gly Gly Asp Pro ile Thr
565 570 575	370 375 380
15 Ile Asn Gly Lys Lys Glu Ala Gly Ile Pro Glu Phe Tyr Asp	15 Pro Asp Asp Val Pro Pro Glu Gly Trp Asn Arg Thr Arg His Val Ile
545 550 555 560	355 360 365
Lys Arg Asp Leu Glu Ile Glu Val Val Leu Phe His Pro Asn Tyr Asn	Thr Asn Thr Lys Lys Ala Leu Gln Ala Val Tyr Ser Met Met Ser Trp
530 535 540	340 345 350
Thr Val Asp Lys Glu His Ser Ile Lys Val Ser Val Gly Gly Glu	Lys Gln Leu Asn Glu Ile Asn Tyr Glu Asp His Lys Leu Lys Ser Gly
10 515 520 .525	325 330 335
Gly Ala Val Val Ser Glu Tyr Phe Val Leu Thr Ala Ala His Cys Phe	Trp Val Lys Val Ser Glu Ala Asp Ser Ser Așn Ala Asp Trp Val Thr
500 505 510	305 310 315 320
Ala Lys Ile Ser Val Ile Arg Pro Ser Lys Gly His Glu Ser Cys Met	Val Lys Pro Arg Tyr Gly Leu Val Thr Tyr Ala Thr Tyr Pro Lys Ile
485 490 495	290 295 300 .
5 Val Trp Glu His Arg Lys Gly Thr Asp Tyr His Lys Gln Pro Trp Gln	5 Ala Lys Lys Cys Leu Val Asn Leu Ile Glu Lys Val Ala Ser Tyr Gly
465 470 . 475 . 480	275 280 285
Phe Tyr Gln Met Ile App Glu Ser Gln Ser Leu Ser Leu Cys Gly Met	Leu Val Leu Asp Gly Ser Asp Ser Ile Gly Ala Ser Asn Phe Thr Gly
450 455 460	260 265 270
Glu Gln His Val Phe Lys Val Lys Asp Met Glu Asn Leu Glu Asp Val	Gln Lys Arg Lys Ile Val Leu Asp Pro Ser Gly Ser Met Asn Ile Tyr
WO 2004/055519 PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057

WO 2004/05S519 PCT/EP2003/014057 15/335	WO 2004/055519 PCT/EP2003/014057
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675 680 685	1 5 10 · 15
Tyr Ala Asp Pro Asn Thr Cys Arg Gly Asp Ser Gly Gly Pro Leu Ile	Ser Ala Gly Asn Gly Ala Gly Gly Gly Ser Met Gly Asp Tyr Met
	. 20 25 . 30
Val His Lys Arg Ser Arg Phe 11e Gln Val Gly Val 11e Ser Trp Gly	Ala Gln Glu Asp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp
10 705 710 715 720	10 35 40 . 45
Val Val Asp Val Cys Lys Asn Gln Lys Arg Gln Lys Gln Val Pro Ala	Glu Lys Gln Gln Arg Lys Thr Phe Thr Ala Try Cys Asn Ser His Leu
725 730 735	09 55 05
His Ala Arg Asp Phe His Ile Asn Leu Phe Gln Val Leu Pro Trp Leu	Arg Lys Ala Gly Thr Gln Ile Glu Asn Ile Asp Glu Asp Phe Arg Asp
740 745 750	65 70 75 80
15 Lys Glu Lys Leu Gln Asp Glu Asp Leu Gly Phe Leu	15 Gly Leu Lys Leu Met Leu Leu Glu Val Ile Ser Gly Glu Arg Leu
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	Pro Lys Pro Glu Arg Gly Lys Met Arg Val His Lys Ile Asn Asn Val
	. 100 105
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20 <211> 911	20 115 120 125
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WO 2004/055519 PCT/EP2003/014057 17/335	Glu Glu Thr Ser Ala Lys Glu Gly Leu Leu Leu Trp Cys Gln Arg Lys	165 170 175	Thr Ale Pro Tyr Lys Asn Val Asn Val Gln Asn Phe His Ile Ser Trp	180 185 190	Lys Asp Gly Leu Ala Phe Asn Ala Leu Ile His Arg His Arg Pro Glu	195 200 205	Leu Ile Glu Tyr Asp Lys Leu Arg Lys Asp Asp Pro Val Thr Asn Leu	210 215 220	Asn Asn Ale Phe Glu Val Ala Glu Lys Tyr Leu Asp Ile Pro Lys Met	225 230 . 235 240	Leu Asp Ala Glu Asp Ile Val Asn Thr Ala Arg Pro Asp Glu Lys Ala	. 255 255	Ile Met Thr Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly Ala Gin	260 265 270	Lys Ala Glu Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala Val Asn	275 280 285	Gln Glu Aen Glu His Leu Met Glu Asp Tyr Glu Lys Leu Ala Ser Asp	290 295 300	Leu Leu Glu Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asp Arg Val	305 310 315 320	Pro Gln Lys Thr Ile Gln Glu Met Gln Gln Lys Leu Glu Asp Phe Arg	325 330 335	Asp Tyr Arg Arg Val His Lys Pro Pro Lys Val Gln Glu Lys Cys Gln	340 345 350

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		19/335		20/335	
	Glu Ser Ale Met Glu Asp Leu Gln Asp Met Phe Ile	In Asp Met Phe Ile Val	His Thr Ile	Glu Gln Leu Leu Thr Thr Ile Ala Arg Thr Ile Asn Glu Val Glu Asn	Glu Asn
	545 550	. 555	095	740 745 750	
	Glu Glu Ile Glu Gly Leu Ile Ser Ala His Asp Gln		Phe Lys Ser Thr	Gln lle Leu Thr Arg Asp Ala Lys Gly Ile Ser Gln Glu Gln Met Gln	Met Gln
		570	575	755 . 097	
S	Leu Pro Asp Ala Asp Arg Glu Arg Glu Ala Ile Leu		Ala Ile His Lys	5 Glu Phe Arg Ala Ser Phe Aen His Phe Asp Lys Asp His Gly Gly Ala	Gly Ala
	580	585		770 775 780	
	Glu Ala Gln Arg Ile Ala Glu Ser Asn His Ile Lys	er Asn His Ile Lys Leu	1 Ser Gly Ser	Leu Gly Pro Glu Glu Phe Lys Ala Cys Leu Ile Ser Leu Gly Tyr Asp	Tyr Asp
	295	600 605		785 790 795	800
	Asn Pro Tyr Thr Thr Val Thr Pro Gln Ile Ile Asn		Ser Lys Trp Glu	Val Glu Asn Asp Arg Gln Gly Glu Ala Glu Phe Asn Arg Ile Met Ser	Met Ser
10	610 615	620		10 805 810	815
	Lys Val Gin Gin Leu Val Pro Lys Arg Asp His Ala		Leu Leu Glu Glu	Leu Val Asp Pro Asn His Ser Gly Leu Val Thr Phe Gln Ala Phe Ile	Phe Ile
	625 630	635		820 825 830	
	Gln Ser Lys Gln Gln Sex Asn Glu His Leu Arg Arg		Gln Phe Ala Ser	Asp Phe Met Ser Arg Glu Thr Thr Asp Thr Asp Thr Ala Asp Gln Val	Gln Val
	645	650	655	835 840 · 845	
13	Gln Ala Asn Val Val Gly Pro Trp Ile Gln Thr Lys		Met Glu Glu Ile	15 Ile Ala Ser Phe Lys Val Leu Ala Gly Asp Lys Asn Phe Ile Thr Ala	Thr Ala
	099	665	670	098 558 058)
	Gly Arg Ile Ser Ile Glu Met Asn Gly Thr Leu Glu		Asp Gln Leu Ser	Glu Glu Leu Arg Arg Glu Leu Pro Pro Asp Gln Ala Glu Tyr Cys Ile	. Cys Ile
	. 675	10 685		865, 870 875	. 880
	His Leu Lys Gln Tyr Glu Arg Ser Ile Val Asp Tyr		Lys Pro Asn Leu	Ala Arg Met Ala Pro Tyr Gln Gly Pro Asp Ala Val Pro Gly Ala Leu	Ala Leu
20	569 069	700		20 885 890	895
	Asp Leu Leu Glu Gln Gln His Gln Leu Ile Gln Glu		Ala Leu Ile Phe	Asp Tyr Lys Ser Phe Ser Thr Ala Leu Tyr Gly Glu Ser Asp Leu	Leu
	705 710	715	720	900 905 910	
	Asp Asn Lys His Thr Asn Tyr Thr Met Glu His Ile		Arg Val Gly Trp	* * * * * * * * * * * * * * * * * * * *	
	725	730	735		

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- -211> 683	115 120	125
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<213> Homo sapiens	130 135	140
5 <220>	5 Asn Glu Ala Trp Ala Ser Leu Pro Ala Glu Val Leu Asp Ser Leu Val	Val Leu Asp Ser Leu Val
<221> Transforming growth factor-beta induced protein IG-H3 precursor	1.45 150	155 160
<222> (1)(683)	Ser Asn Val Asn Ile Glu Leu Leu Asn Ala Leu Arg Tyr His Met Val	Leu Arg Tyr His Met Val
<223> Accession No. as of 06 Dec 2002: Q15582	165	175
9 <000>	Gly Arg Arg Val Leu Thr Asp Glu Leu Lys His Gly Met Thr Leu Thr	His Gly Met Thr Leu Thr
01	. 10 180 185	190
Met Ala Leu Phe Val Arg Leu Leu Ala Leu Ala Leu Ala Leu	Ser Met Tyr Gln Asn Ser Asn Ile Gln Ile His Hyr Pro Asn Gly	His His Tyr Pro Asn Gly
1 5 10 15	195 200	205
Gly Pro Ala Ala Thr Leu Ala Gly Pro Ala Lys Ser Pro Tyr Gln Leu	Ile Val Thr Val Asn Cys Ala Arg Leu Leu Lys Ale Asp His His Ale	Lys Ala Asp His His Ala
20 25 30	210 215	220
15 Val Leu Gln His Ser Arg Leu Arg Gly Arg Gln His Gly Pro Asn Val	15 Thr Asn Gly Val Val His Leu Ile Asp Lys Val Ile Ser Thr Ile Thr	Val Ile Ser Thr Ile Thr
35 . 40 45	225 230	235 240
Cys Ala Val Gln Lys Val Ile Gly Thr Asn Arg Lys Tyr Phe Thr Asn	Asn Asn Ile Gln Gln Ile Ile Glu Ile Glu Asp Thr Phe Glu Thr Leu	Asp Thr Phe Glu Thr Leu
50 55 60	245 250	. 255
Cys Lys Gln Trp Tyr Gln Arg Lys Ile Cys Gly Lys Ser Thr Val Ile	Arg Ala Ala Val Ala Ala Ser Gly Leu Asn Thr Met Leu Glu Gly Asn	Thr Met Leu Glu Gly Asn
20 65 70 75 80	20 260 265	270
Ser Tyr Glu Cys Cys Pro Gly Tyr Glu Lys Val Pro Gly Glu Lys Gly	Gly Gln Tyr Thr Leu Leu Ala Pro Thr Asn Glu Ala Phe Glu Lys Ile	Glu Ala Phe Glu Lys Ile
	275 280	. 582
Cys Pro Ala Ala Leu Pro Leu Ser Asn Leu Tyr Glu Thr Leu Gly Val	Pro Ser Glu Thr Leu Asn Arg Ile Leu Gly Asp Pro Glu Ala Leu Arg	Asp Pro Glu Ala Leu Arg
100 . 105 110	. 290 295 .	. 300

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		23/335		24/335	
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	305	310 315	320	500 505 510	
	Ile Val Ala Gl	ile Val Ala Gly Leu Ser Val Glu Thr Leu Glu Gly Thr Thr Leu Glu	Thr Thr Leu Glu	Asn Arg Phe Ser Met Leu Val Ala Ala Ile Gln Ser Ala Gly Leu	u Thr
		325 330	335	515 520 525	
٠,		Val Gly Cys Ser Gly Asp Met Leu Thr Ile Asn Gly Lys Ala Ile Ile		5. Glu Thr Leu Asn Arg Glu Gly Val Tyr Thr Val Phe Ala Pro Thr Asn	Ľ Asn
	340	345	. 056	530 535 540	
	Ser Asn Lys Ası	Ser Asn Lys Asp Ile Leu Ala Thr Asn Gly Val Ile His Tyr Ile Asp	His Tyr Ile Asp	Glu Ala Phe Arg Ala Leu Pro Pro Arg Glu Arg Ser Arg Leu Leu Gly	n Gly
	355	360	365	545 550 555	260
	Glu beu beu Ile	Glu Leu Leu Ile Pro Asp Ser Ala Lys Thr Leu Phe Glu Leu Ala Ala	Glu Leu Ala Ala	Asp Ala Lys Glu Leu Ala Asn Ile Leu Lys Tyr His Ile Gly Asp Glu	n Glu
9	370	375 380	01	565 570 575	٠ يم
	Glu Ser Asp Val	Glu Ser Asp Val Ser Thr Ala Ile Asp Leu Phe Arg Gl	Gln Ala Gly Leu	ile Leu Val Ser Gly Gly Ile Gly Ala Leu Val Arg Leu Lys Ser Leu	r Leu
	385	390 395		065 . 585 . 085	
	Gly Asn His Let	Gly Asn His Leu Ser Gly Ser Glu Arg Leu Thr Leu Leu Ala Pro Leu	Leu Ala Pro Leu	Gln Gly Asp Lys Leu Glu Val Ser Leu Lys Asn Asn Val Val Ser Val	r Val
		405 410	415	295 600 605	
15		Asn Ser Val Phe Lys Asp Gly Thr Pro Pro Ile Asp Al	Ala His Thr Arg	5 Asn Lys Glu Pro Val Ala Glu Pro Asp Ile Met Ala Thr Asn Gly Val	y Val
	420	425	430	610 615 620	
	Asn Leu Leu Arg	Asn Leu Leu Arg Asn His Ile Ile Lys Asp Gln Leu Al	Ala Ser Lys Tyr	Val His Val Ile Thr Asn Val Leu Gin Pro Pro Ala Asn Arg Pro	o Gln
	435	440	445	625 630 635	640
	Leu Tyr His Gly	Leu Tyr His Gly Gln Thr Leu Glu Thr Leu Gly Gly Ly	Lys Lys Leu Arg	Glu Arg Gly Asp Glu Leu Ala Asp Ser Ala Leu Glu Ile Phe Lys Gln	s Gln
20	450	455 460		. 645 . 650 . 655	s.
	Val Phe Val Tyr	Val Phe Val Tyr Arg Asn Ser Leu Cys Ile Glu Asn Ser	Ser Cys Ile Ala	Ala Ser Ala Phe Ser Arg Ala Ser Gln Arg Ser Vel Arg Leu Ala Pro	a Pro
	465	470 475		660 665 670	
	Ala His Asp Lys	Ala His Asp Lys Arg Gly Arg Tyr Gly Thr Leu Phe Thr	Thr Met Asp Arg	Val Tyr Gln Lys Leu Leu Glu Arg Met Lys His	
		485 . 490	967	675 680	

	WO 2004/055519	25/335	PCT/EP2003/014057	WO 2004/055519 26/335	PCT/EP2003/01405
				Leu Asp Phe Ile Ala Ser Lys Gly Val Lys Leu Val Ser Ile Gly Ala	Leu Val Ser Ile Gly Ala
				100	110
	<210> 7			Glu Glu Ile Val Amp Gly Amn Val Lym Met Thr Leu Gly Met Ile	Thr Leu Gly Met Ile Trp
	<211> 892			115 120	125
2	<212> PRT		.,	5 Thr ile ile Leu Arg Phe Ala ile Gin Asp ile Ser Val Glu Glu Thr	Ile Ser Val Glu Glu Thr
	<213> Homo sapiens			130 135	140
	<220>			Ser Ala Lys Glu Gly Leu Leu feu Trp Cys Gln Arg Lys Thr Ala Pro	Gln Arg. Lys Thr Ala Pro
	<221> Alpha-actinin 1			145 150	155 .160
	<222> (1)(892)			Tyr Lys Asn Val Asn Ile Gin Asn Phe His Ile Ser Trp Lys Asp Gly	lle Ser Trp Lys Asp Gly
01	<223> Accession No. P12814). P12814		165	. 175
	<400> 7			Leu Gly Phe Cys Ala Leu Ile His Arg His Arg Pro Glu Leu Ile Asp	Arg Pro Glu Leu Ile Asp
				180 185	190
	Met Asp His Tyr Asp	Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met	iet Gln Pro Glu	Tyr Gly Lys Leu Arg Lys Asp Asp Pro Leu Thr Asn Leu Asn Thr Ala	Thr Asn Leu Asn Thr Ala
	1 5	10	. 15	195 200	205
15		Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln	o Glu Lýs Gln 15	5 Phe Asp Val Ala Glu Lys Tyr Leu Asp Ile Pro Lys Met Leu Asp Ala	Pro Lys Met Leu Asp Ala
	20		30	210 215	220
·	Gln Arg Lys Thr Phe	Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala	Arg Lys Ala	Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu Lys Ala Ile Met Thr	Glu Lys Ala Ile Met Thr
	35	40 45		225 230	235 240
	Gly Thr Gln Ile Glu	Gly Thr Gin Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys) Gly Leu Lys	Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly Ala Gln Lys Ala Glu	Gly Ala Gln Lys Ala Glu
70	50	25 60	20	245 250	255
	Leu Met Leu Leu Leu	Leu Met Leu Leu Leu Glu Val Ile Ser Gly Glu Arg Leu	eu Ala Lys Pro	Thr Ale Ale Aen Arg Ile Cye Lye Val Leu Ale Vel Aen Gln Glu Aen	Ale Val Asn Gln Glu Asn
	65	70 75	80	260 . 265	270
	Glu Arg Gly Lys Met	Glu. Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val	al Asn Lys Ala	Glu Gin Leu Met Glu Asp Tyr Glu Lys Leu Ala Ser Asp Leu Leu Glu	Ala Ser Asp Leu Leu Glu
		06	95	275 280	285

WO 2004/055519 PCT/EP2003/014057 28/335	Asp Gln Trp Asp Asn Leu Gly Ala Leu Thr Gln Lys Arg Arg Glu Ala	485 490 495	Leu Glu Arg Thr Glu Lys Leu Leu Glu Thr Ile Asp Gln Leu	500 505 510	5 Glu Tyr Ala Lys Arg Ala Ala Pro Phe Asn Asn Trp Met Glu Gly Ala	515 520 525	Met Glu Asp Leu Gln Asp Thr Phe Ile Val His Thr Ile Glu Glu Ile	530 535 . 540	Gln Gly Leu Thr The Ala His Glu Gln Phe Lys Ala Thr Leu Pro Asp	10 545 550 555 560	Ala Asp Lys Glu Arg Leu Ala Ile Leu Gly Ile His Asn Glu Val Ser	565 570 575	Lys Ile Val Gln Thr Tyr His Val Asn Met Ala Gly Thr Asn Pro Tyr	280 585 280	15 Thr Thr Ile Thr Pro Gln Glu Ile Asn Gly Lys Trp Asp His Val Arg	209 009 265	Gln Leu Val Pro Arg Arg Asp Gln Ala Leu Thr Glu Glu His Ala Arg	610 615 620	Gln Gln His Asn Glu Ser Val Arg Lys Gln Phe Gly Ale Gln Ale Asn	20 625 . 630 . 635 640	Val Ile Gly Pro Trp Ile Gln Thr Lys Met Glu Glu Ile Gly Arg Ile	645 650 655	Ser Ile Glu Met His Gly Thr Leu Glu Asp Gln Leu Ser His Leu Arg
PCT/EP2003/014057	Pro Glu Asn		Asp Tyr Arg	320	Leu Glu İle	335	Arg Pro Ala	350	Asn Ala Trp		Leu Leu Asn		Lys Phe Arg	400	Glu Ala Met	415	lle Lys Ala	430	Ale His Gln		Asn Glu Leu		Lys Ile Cys
27/335	Trp lle Arg Arg Thr 11e Pro Trp Leu Glu Asn Arg Val Pro	300	eu Glu Asp Phe Arg	315	ln Glu Lys Cys Gln	330	eu Arg Leu Ser Asn	345	al Ser Asp Ile Asn	365	lly Tyr Glu Glu Trp	380	sp His Leu Ala Glu	395	rp Thr Asp Gly Lys	410	la Thr Leu Ser Glu	425	lu Ser Asp Leu Ala	445	le Ala Gin Giu Leu	460	sn Ala Arg Cys Gln
27,	g Thr Ile Pro Trp 1	295	Thr Met His Ala Met Gln Gln Lys Leu Glu Asp Phe Arg Asp	310	Arg Leu His Lys Pro Pro Lys Val Gin Glu Lys Cys Gin Leu	325	Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu Ser Asn Arg		Phe Met Pro Ser Glu Gly Arg Met Val Ser Asp Ile Asn Asn	360	Gly Cye Leu Glu Gln Vel Glu Lys Gly Tyr Glu Glu Txp Leu	375	Glu ile Arg Arg Leu Glu Arg Leu Asp His Leu Ala Glu Lys	390	Gln Lys Ala Ser Ile His Glu Ala Trp Thr Asp Gly Lys Glu	405	Leu Arg Gln Lys Asp Tyr Glu Thr Ala Thr Leu Ser Glu Ile		Leu Leu Lys Lys His Glu Ala Phe Glu Ser Asp Leu Ala Ala	440	Asp Arg Val Glu Gln Ile Ala Ala Ile Ala Gln Glu Leu Asn	455	Asp Tyr Tyr Asp Ser Pro Ser Val Asn Ala Arg Cys Gln Lys
	•		R		ē. Ž		an Tr	340	Pro Se	355	Leu Gl		Arg Ar		Ala Se		Gln Ly	420	Гув Гу	435	Val Gl		yr As

WO 2004/055519 30/335 30/335 Ala Pro Tyr Thr Gly Pro And Ser Val Pro Gly ala Leu and Tyre Web	And fig. 197 this 619 ftd Aby Ser var fro 619 And Lett Aby 197 Met	865 . 870 875 880	Ser Phe Ser Thr Ala Leu Tyr Gly Glu Ser Asp Leu		so		<210> 8	<211> 448	<212> PRT	10 <213> Homo sapiens	<220>	<221> Tubulin alpha-4 chain	<222> (1)(448)	<223> Accession No. P05215	15 <400> B		Met Arg Glu Cye Ile Ser Val His Val Gly Gln Ala Gly Val Gln Met	1 , 5 10 15	Gly Asn Ala Cys Trp Glu Leu Tyr Cys Leu Glu His Gly Ile Gln Pro	20 20 25 30	Asp Gly Gln Met Pro Ser Asp Lys Thr Ile Gly Gly Asp Asp Ser	35 40 45	Phe Thr Thr Phe Phe Cys Glu Thr Gly Ala Gly Lys His Val Pro Arg	90 85 60		
WO 2004/055519 29/335 29/335 29/335 29/335 29/335 29/335	yr bys fro bys ite	675 680 685	Glu Gly Asp His Gln Leu Ile Gln Glu Ala Leu Ile Phe Asp Asn Lys	690 695 700	5 His Thr Asn Tyr Thr Met Glu His Ile Arg Val Gly Trp Glu Gln Leu	705 710 715 720	Leu Thr Thr Ile Ala Arg Thr Ile Asn Glu Val Glu Asn Gln Ile Leu	725 730 735	Thr Arg Asp Ala Lys Gly Ile Ser Gin Glu Gin Met Asn Glu Phe Arg	10 740 745 750	Ala Ser Phe Asn His Phe Asp Arg Asp His Ser Gly Thr Leu Gly Pro	755 760 765	Glu Glu Phe Lys Ala Cys Leu Ile Ser Leu Gly Tyr Asp Ile Gly Asn	770 775 780	15 Asp Pro Gln Gly Glu Ala Glu Phe Ala Arg Ile Met Ser Ile Val Asp	795 800	Pro Asn Arg Leu Gly Val Val Thr Phe Gln Ala Phe Ile Asp Phe Met	805 810 815	Ser Arg Glu Thr Ala Asp Thr Asp Thr Ala Asp Gln Val Met Ala Ser	20 820 825 830	Phe Lys Ile Leu Ala Gly Asp Lys Asn Tyr Ile Thr Met Asp Glu Leu	835 840 845	Arg Arg Glu Leu Pro Pro Asp Gln Ala Glu Tyr Cys Ile Ala Arg Met	. 098 855		

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Ala Val Phe Val Asp Leu Glu Pro Thr Val Ile Asp Glu Ile Arg Asn	Thr Asn Leu Val Pro Tyr Pro Arg Ile His Phe Pro Leu Ala Thr Tyr
. 75 80	260 265 270
Gly Pro Tyr Arg Gln Leu Phe His Pro Glu Gln Leu Ile Thr Gly Lys	Ala Pro Val Ile Ser Ala Glu Lys Ala Tyr His Glu Gln Leu Ser Val
	275 280 285
5 Glu Asp Ala Asa Asa Asa Tyr Ala Arg Gly His Tyr Thr Ile Gly Lys	5 Ala Glu Ile Thr Asn Ala Cys Phe Glu Pro Ala Asn Gln Met Val Lys
100 105 110	290 295 300
Glu Ile Ile Asp Pro Val Leu Asp Arg Ile Arg Lys Leu Ser Asp Gln	Cys Asp Pro Arg His Gly Lys Tyr Met Ala Cys Cys Leu Leu Tyr Arg
115 120 125	305 310 315 320
Cys Thr Gly Leu Gln Gly Phe Leu Val Phe His Ser Phe Gly Gly Gly	Gly Asp Val Val Pro Lys Asp Val Asn Ala Ala Ile Ala Ala Ile Lys
10 130 135 140	10 325 330 335
Thr Gly Ser Gly Phe Thr Ser Leu Leu Met Glu Arg Leu Ser Val Asp	Thr Lys Arg Ser Ile Gln Phe Val Asp Trp Cys Pro Thr Gly Phe Lys
145 150 155 160	340 345 350
Tyr Gly Lys Lys Lys Leu Glu Phe Ser Ile Tyr Pro Ala Pro Gln	Val Gly lle Asn Tyr Gln Pro Pro Thr Val Val Pro Gly Gly Asp Leu
165 170 175	355 360 365
15 Val Ser Thr Ala Val Val Glu Pro Tyr Asn Ser Ile Leu Thr Thr His	15 Ala Lys Val Gin Arg Ala Val Cys Met Leu Ser Asn Thr Thr Ala Ile
. 180 185 190	370 375 380
Thr Thr Leu Glu His Ser Asp Cys Ala Phe Met Val Asp Asn Glu Ala	Ala Glu Ala Trp Ala Arg Leu Asp His Lys Phe Asp Leu Met Tyr Ala
195 200 . 205	395 . 390 . 395
ile Tyr Asp ile Cys Arg Arg Asn Leu Asp ile Glu Arg Pro Thr Tyr	Lys arg ala the Val His Trp Tyr Val Gly Glu Gly Met Glu Glu Gly
20 210 215 220	20 405 410 415
Thr Asn Leu Asn Arg Leu lle Ser Gln 11e Val Ser Ser 11e Thr Ala	Glu Phe Ser Glu Ala Arg Glu Asp Met Ala Ala Leu Glu Lys Asp Tyr
225 230 . 235 240	420 425 430
Ser Leu Arg Phe Asp Gly Ala Leu Asn Val Asp Leu Thr Glu Phe Gln	Glu Glu Val Gly Ile Asp Ser Tyr Glu Asp Glu Asp Glu Gly Glu Glu
245 250 255	435 440 445

S6 06 .
Leu Glu Val Leu. Ser Gln Lys Lys Met His Arg Lys His Asn Gln Arg
65 70 75 80
Ala Asn Leu Gin Thr Asp Leu Ser Asp Gly Leu Arg Leu Ile Ala Leu
20 50 55 . 60
Phe Thr Arg Trp Cys Asn Glu His Leu Lys Cys Val Ser Lys Arg Ile
35 40 45
Lys Asp Leu Ala Glu Asp Ala Pro Trp Lys Lys Ile Gln Gln Asn Thr
. 20 25 30
15 Pro Gly Gly Gly Val Asp Thr Arg Asp Ala Glu Met Pro Ala Thr Glu
1 5 10 . 15
Met Ser Ser His Ser Arg Ala Gly Gln Ser Ala Ala Gly Ala Ala
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Pro Gly Ile Glu Pro Thr Gly Asn Met Val Lys Lys Arg Ala Glu Phe	ser Ala Cys Arg Ala Val Gly Arg Gly Leu Gln Pro Lys Gly Val Arg
290 295 300	485 490 495
Thr Val Glu Thr Arg Ser Ala Gly Glu Gly Glu Val Leu Val Tyr Val	Val Lys Glu Thr Ala Asp Phe Lys Val Tyr Thr Lys Gly Ala Gly Ser
305 310 315 320	500 505 510 .
5 Glu Asp Pro Ala Gly His Gln Glu Glu Ala Lys Val Thr Ala Asn Asn	5 Gly Glu Leu Lys Val Thr Val Lys Gly Pro Lys Gly Glu Glu Arg Val
325 330 335	515 520 525
Asp Lys Asn Arg Thr Phe Ser Val Trp Tyr Val Pro Glu Val Thr Gly	Lys Gln Lys Asp Leu Gly Asp Gly Val Tyr Gly Phe Glu Tyr Tyr Pro
340 345 350	530 535 540
Thr His Lys Val Thr Val Leu Phe Ala Gly Gln His Ile Ala Lys Ser	Met Val Pro Gly Thr Tyr Ile Val Thr Ite Thr Trp Gly Gly Gln Asn
10 355 360 365	10 545 550 555 560
Pro Phe Glu Val Tyr Val Asp Lys Ser Gln Gly Asp Ala Ser Lys Val	ile Gly Arg Ser Pro Phe Glu Val Lys Val Gly Thr Glu Cys Gly Asn
370 375 380	565 570 575
Thr Ala Gln Gly Pro Gly Leu Glu Pro Ser Gly Asn Ile Ala Asn Lys	Gln Lys Val Arg Ala Trp Gly Pro Gly Leu Glu Gly Gly Val Val Gly
385 390 400	585 590
15 Thr Thr Tyr Phe Glu Ile Phe Thr Ala Gly Ala Gly Thr Gly Glu Val	15 Lys Ser Ala Asp Phe Val Val Glu Ala Ile Gly Asp Asp Val Gly Thr
405 410 415	509 009 565
Glu Val Val Ile Gln Asp Pro Met Gly Gln Lys Gly Thr Val Glu Pro	Leu Gly Phe Ser Val Glu Gly Pro Ser Gln Ala Lys Ile Glu Cys Asp
420 425 430	610 615 620
Gln Leu Glu Ala Arg Gly Asp Ser Thr Tyr Arg Cys Ser Tyr Gln Pro	Asp Lys Gly Asp Gly Ser Cys Asp Val Arg Tyr Trp Pro Gln Glu Ala
20 435 440 445	20 625 630 635 640
Thr Met Glu Gly Val His Thr Val His Val Thr Phe Ala Gly Val Pro	Gly Glu Tyr Ale Val His Val Leu Cys Asn Ser Glu Asp Ile Arg Leu
450 455 460	. 650 650 .
ile Pro Arg Ser Pro Tyr Thr Val Thr Val Gly Gln Ala Cys Asn Pro	Ser Pro Phe Met Ala Asp Ile Arg Asp Ala Pro Gln Asp Phe His Pro
465 470 475 . 480 .	660 665 670

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	Asp Arg Val Lys Ala Arg Gly Pro Gly Leu Glu Lys Thr	Leu Glu Lys Thr Gly Val Ala	Lys Val Glu Pro Ser His Asp Ala Ser Lys Val Lys Ala Glu Gly Pro	ly Pro
	675 680	. 685	. 865 870 875	880
	Vel Asn Lys Pro Ala Glu Phe Thr Val Asp Ala Lys His	Asp Ala Lys His Gly Gly Lys	Gly Leu Ser Arg Thr Gly Val Glu Leu Gly Lys Pro Thr His Phe Thr	he Thr
	969 069	700	885 890	
'n	Ala Pro Leu Arg Val Gln Val Gln Asp Asn Glu Gly	Asn Glu Gly Cys Pro Val Glu	5 Val Asn Ala Lys Ala Ala Gly Lys Gly Lys Leu Asp Val Gln Phe Ser	he Ser
	705 710	715 720	900 905 910	
	Ala Leu Val Lys Asp Asn Gly Asn Gly Thr Tyr Ser Cys	Thr Tyr Ser Cys Ser Tyr Val	Gly Leu Thr Lys Gly Asp Ala Val Arg Asp Val Asp Ile Ile Asp His	sp His
	725	730 735	915 920 925	
	Pro Arg Lys Pro Val Lys His Thr Ala Met Val Ser Trp	Met Val Ser Trp Gly Gly Val	His Asp Asn Thr Tyr Thr Val Lys Tyr Thr Pro Val Gln Gln Gly Pro	ly Pro
10	740 745	750	10 930 935 940	
	Ser Ile Pro Asn Ser Pro Phe Arg Val Asn Val Gly Ala	Asn Val Gly Ala Gly Ser His	Val Gly Val Asn Val Thr Tyr Gly Gly Asp Pro Ile Pro Lys Ser Pro	er Pro
	092	765	945 950 955	. 096
	Pro Asn Lys Val Lys Val Tyr Gly Pro Gly Val Ala Lys Thr Gly Leu	Gly Val Ala Lys Thr Gly Leu	Phe Ser Val Ala Val Ser Pro Sor Leu Asp Leu Ser Lys Ile Lys Val	ys Val
	770 775	780	965 970 975	75
15	Lys Ala His Glu Pro Thr Tyr Phe Thr Val Asp Cys Ala Glu Ala Gly	Val Asp Cys Ala Glu Ala Gly	is Ser Gly Leu Gly Glu Lys Val Asp Val Gly Lys Asp Gln Glu Phe Thr	he Thr
	785 790	795	986 986	
	Gln Gly Asp Val Ser Ile Gly Ile Lys Cys Ala Pro Gly Val Val Gly	Cys Ala Pro Gly Val Val Gly	Val Lys Ser Lys Gly Ala Gly Gly Gly Lys Val Ala Ser Lys Ile	Lys Ile
	805	. 810 815	995 1000 1005	
	Pro Ala Glu Ala Asp Ile Asp Phe Asp Ile Ile Arg Asn Asp Asn Asp	lle lle Arg Asn Asp Asn Asp	Val Gly Pro Ser Gly Ala Ala Val Pro Cys Lys Val Glu Pro Gly	· Gly
70	820 825	830	.20 1010 1015 1020	
	Thr Phe Thr Val Lys Tyr Thr Pro Arg Gly Ala Gly Ser Tyr Thr Ile	Gly Ala Gly Ser Tyr Thr Ile	Leu Gly Ala Asp Asn Ser Val Val Arg Phe Leu Pro Arg Glu Glu	n Glu
	835 840	845	1025 1030 1035	
	Met Val Leu Phe Ala Asp Gln Ala Thr Fro Thr Ser Pro Ile Arg Val	Pro Thr Ser Pro 11e Arg Val	Gly Pro Tyr Glu Val Glu Val Thr Tyr Amp Gly Val Pro Val Pro	l Pro
	850 855		1040 1045 1050	

	WO 2004/055519	(5519		PCT/EP2003/014057	WO JOSHOKKETO		•	
			39/335		CTCCCOILOGT O	\$61/07		PCT/EP2003/0
	,	:				666104	•	
	Gly Ser	Pro Phe Pro Leu Glu	Ala Val Ala Pro Thr	Lys Pro Ser	Lys Tyr Gly Gly Gln Pro Val	o Val Pro Asn Phe Pro Ser		Lys Leu Gln
	1055	1060	1065		1235	1240	1245	
	Lys Val	Lys Ala Phe Gly Pro	Gly Leu Gln Gly Gly	Ser ala Gly	Val Glu Pro Ala Val Asp Thr	p Thr Ser Gly Val Gln Cys Tyr Gly Pro	n Cys Tyr	Gly Pro
	1070	1075	1080		1250	1255	1260	
r.	Ser Pro	Ala Arg Phe Thr Ile	Asp Thr Lys Gly Ala	Gly Thr Gly 5	Gly lle Glu Gly Gln Gly Vel Phe Arg Glu Ala Thr Thr Glu Phe	y Val Phe Arg Glu Al	a Thr Thr	Glu Phe
	1085		1095		.1265	1270	1275	
	Gly Leu	Gly Leu Thr Val Glu Gly Pro Cys Glu	Ala	Gln Leu Glu	Ser Val Asp Ala Arg Ala Leu Thr Gln Thr Gly Gly Pro His Val	a Leu Thr Gln Thr Gl <u>ı</u>	y Gly Pro	His Val
	1100	1105	1110		1280	1285	1290	
	Сув Ьец	Asp Asn Gly Asp Gly	Thr Cys Ser Val Ser	Tyr Val Pro	Lys Ala Arg Val Ala Asn Pro	n Pro Ser Gly Asn Leu Thr		Glu Thr Tyr
2	1115	1120	1125	ot	1295	1300	1305	
	Thr Glu	Pro Gly Asp Tyr Asn	Ile Asn Ile Leu Phe	Ala Asp Thr	Val Gln Asp Arg Gly As	Asp Arg Gly Asp Gly Met Tyr Lys Val Glu Tyr Thr Pro	l Glu Tyr	Thr Pro
	1130	1135	1140	• .	1310	1315	1320	
	His Ile	Pro Gly Ser Pro Phe	Lys Ala His Val Val	Pro Cys Phe	Tyr Glu Glu Gly Leu Hi	Glu Gly Leu His Ser Val Asp Val Thr Tyr		Asp Gly Ser
	1145	1150	. 1155		1325	1330	1335	
15	Asp Ala	Ser Lys Val Lys Cys	Ser Gly Pro Gly Leu (Glu Arg Ala	Pro Val Pro Ser Ser Pro Phe	Phe Gin Val Pro Val Thr	_ •	Glu Gly Cys
	1160	1165	1170		1340	1345	1350	
	Thr Ala	Thr Ala Gly Glu Val Gly Gln Phe Gln Val Asp	23	Ser Ser Ala	Asp Pro Ser Arg Val Ar	Ser Arg Val Arg Val His Gly Pro Gly Ile		Gln Ser Gly
	1175	1180	1185		1355	1360	1365	
	Gly Ser	Gly Ser Ala Glu Leu Thr Ile (Glu Ile Cys Ser Glu	Ala Gly Leu	Thr Thr Asn Lys Pro As	Asn Lys Pro Asn Lys Phe Thr Val Glu Thr		Arg Gly Ala
70	1190	1195	1200	. 02	1370	1375	1380	
	Pro Ala	Glu Val Tyr ile Gln Asp His Gly Asp		Gly The His The	Gly Thr Gly Gly Leu Gl	Gly Gly Leu Gly Leu Ala Val Glu Gly Pro		Ser Glu Ala
	1205	1210	1215		1385	. 1390	1395	
	Ile Thr	Ile Thr Tyr Ile Pro Leu Cys Pro Gly Ala Tyr		Thr Val Thr Ile	Lys Met Ser Cys Met As	Ser Cys Met Asp Asn Lys Asp Gly Ser Cys		Ser Val Glu
	1220	1225	1230		1400	1405	1410	

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WO 2004/055519 PCT/EP2003/014057 42/335			Thr His Ile Gin Asp Asn His Asp Gly Thr Tyr Thr Val Ala Tyr	1595 1600 1605	5 Val Pro Asp Val Thr Gly Arg Tyr Thr Ile Leu Ile Lys Tyr Gly	1610 1615 1620	Gly Asp Glu ile Pro Phe Ser Pro Tyr Arg Val Arg Ala Val Pro	1625 1630 1635	Thr Gly Asp Ala Ser Lys Cys Thr Val Thr Val Ser Ile Gly Gly	. 10 1640 1645 1650	His Gly Leu Gly Ala Gly Ile Gly Pro Thr Ile Gln Ile Gly Glu	1655 1660 1665	Glu Thr Val Ile Thr Val Asp Thr Lys Ala Ala Gly Lys Gly Lys	1670 1675 1680	15 Val Thr Cys Thr Val Cys Thr Pro Asp Gly Ser Glu Val Asp Val	1685 1690 1695	Asp Val Val Glu Asn Glu Asp Gly Thr Phe Asp Ile Phe Tyr Thr	1700 1705 1710	Ala Pro Gln Pro Gly Lys Tyr Val Ile Cys Val Arg Phe Gly Gly	20 1715 1720 1725	Glu His Val Fro Asn Ser Pro Phe Gln Val Thr Ala Leu Ala Gly	1730 1735 1740	Asp Gln Pro Ser Val Gln Pro Pro Leu Arg Ser Gln .Gln Leu Ala	1745 1750 1755
WO 2004/055519 PCT/EP2003/014057 41/335	Tyr ile. Pro Tyr Glu Ala Gly Thr Tyr Ser Leu Asn Val Thr Tyr	1415 1420 1425	Gly Gly His Gln Val Pro Gly Ser Pro Phe Lys Val Pro Val His	1430 1435 1440	5 Asp Val Thr Asp Ala Ser Lys Val Lys Cys Ser Gly Pro Gly Leu	1445 1450 1455	Ser Pro Gly Met Val Arg Ala Asn Leu Pro Gin Ser Phe Gin Val	1460 1465 1470	Asp Thr Ser Lys Ala Gly Val Ala Pro Leu Gln Val Lys Val Gln	10 1475 1480 1485	Gly Pro Lys Gly Leu Val Glu Pro Val Asp Val Val Asp Asn Ala	1490 1495 1500	Asp Gly Thr Gln Thr Val Asn Tyr Val Pro Ser Arg Glu Gly Pro	1505 1510 1515	15 Tyr Ser Ile Ser Val Leu Tyr Gly Asp Glu Glu Val Pro Arg Ser	1520 1525 1530	Pro Phe Lys Val Lys Val Leu Pro Thr His Asp Ala Ser Lys Val	1535 1540 1545	Lys Ala Ser Gly Pro Gly Leu Asn Thr Thr Gly Val Pro Ala Ser	20 1550 1555 1560	Leu Pro Val Glu Phe Thr Ile Asp Ala Lys Asp Ala Gly Glu Gly	. 1565 1570 1575	Leu Leu Ala Val Gln Ile Thr Asp Pro Glu Gly Lys Pro Lys Lys	1580 . 1590

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	Pro Gln	Tyr Thr Tyr Ala Gln	Pro Gln Tyr Thr Tyr Ala Gln Gly Gly Gln Gln Thr Trp Ala Pro	Trp Ala Pro	Asn Glu , Gln His Val Pro Gly	Asn Glu , Gln His Val Pro Gly Ser Pro Phe Thr Ala Arg Val Thr
	1760	1765	5 1770		1940 1945	
	Glu Arg	Pro Leu Val Gly Val	Glu Arg Pro Leu Val Gly Val Asn Gly Leu Asp. Val Thr Ser Leu	Thr Ser Leu	Gly Asp Asp Ser Met Arg Met	Gly Asp Asp Ser Wet Arg Wet Ser His Leu Lys Val Gly Ser Ala
	1775	1780	0 1785		1955 1960	
ď		Phe Asp Leu Val Ile	Arg Pro Phe Asp Leu Val Ile Pro Phe Thr Ile Lys	Lys Gly Glu	5 Ala Asp Ile Pro Ile Asn Ile	Ala Asp ile Pro ile Asn ile Ser Glu Thr Asp Leu Ser Leu Leu
	1790	1795	5 1800		1970	5 1980
	ile Thr	Gly Glu Val Arg Met	Gly Lys Val	Ala Gln Pro	Thr Ala Thr Val Val Pro Pro	Thr Ala Thr Val Val Pro Pro Ser Gly Arg Glu Glu Pro Cyg Leu
	1805	1810	0 1815		1985	0 1995
	Thr Ile	Thr Asp Asn Lys Asp	Thr Ile Thr Asp Asn Lys Asp Gly Thr Val Thr Val	Arg Tyr Ala	Leu Lys Arg Leu Arg Asn Gly	Leu Lys Arg Leu Arg Asn Gly His Val Gly Ile Ser Phe Val Pro
10	1820	1825	5 1830	01	2000 2005	5 2010
	Pro Ser	Glu Ala Gly Leu His	Pro Ser Glu Ala Gly Leu His Glu Met Asp Ile Arg	Tyr Asp Asn	Lys Glu Thr Gly Glu His Leu	Lys Glu Thr Gly Glu His Leu Val His Val Lys Lys Asn Gly Gln
	1835	1840	0		2015 2020	0 2025
	Met His	Ile Pro Gly Ser Pro	Met His Ile Pro Gly Ser Pro Leu Gln Phe Tyr Val	Asp Tyr Val	His Val Ala Ser Ser Pro Ile	His Val Ala Ser Ser Pro Ile Pro Val Val Ile Ser Gln Ser Glu
	1850	1855	1860		2030 2035	. 2040
15	Asn Cys	Gly His Val Thr Ala	Asn Cys Gly His Val Thr Ala Tyr Gly Pro Gly Leu	Thr His Gly 15	i lle Gly Asp Ala Ser Arg Val Arg Val Ser Gly Gln	Arg Val Ser Gly Gln Gly Leu His
	1865	1870	1875		2045 . 2050	0 2055
	Val Val	Asn Lys Pro Ala Thr	Val Val Asn Lys Pro Ala Thr Phe Thr Val Asn Thr	гув Азр Ала	Glu Gly His Thr Phe Glu Pro	Glu Gly His Thr Phe Glu Pro Ala Glu Phe Ile Ile Asp Thr Arg
	1880	1885	1890		2060 2065	5 2070
	Gly Glu	Gly Gly Leu Ser Leu	Gly Glu Gly Gly Leu Ser Leu Ala Ile Glu Gly Pro	Ser Lys Ala	Asp Ala Gly Tyr Gly Gly Leu Ser Leu Ser Ile Glu	Ser Leu Ser Ile Glu Gly Pro Ser
20	1895	1900	1905	20	2075 2080	0 2085
	Glu Ile	Ser Cys Thr Asp Asn	Glu ile Ser Cys Thr Asp Asn Gln Asp Gly Thr Cys	Ser Val Ser	Lys Val Asp Ile Asn Thr Glu	Lys Vel Asp Ile Asn Thr Glu Asp Leu Glu Asp Gly Thr Cys Arg
	1910	1915	1920		2090 2095	5 2100
	Tyr Leu	Pro Val Leu Pro Gly	Tyr Leu , Pro Val Leu Pro Gly Asp Tyr Ser Ile Leu Val	Val Lys Tyr	Val Thr Tyr Cys Pro Thr Glu	Val Thr Tyr Cys Pro Thr Glu Pro Gly Asn Tyr Ile Ile Asn Ile
	1925	1930	1935		2105 2110	0

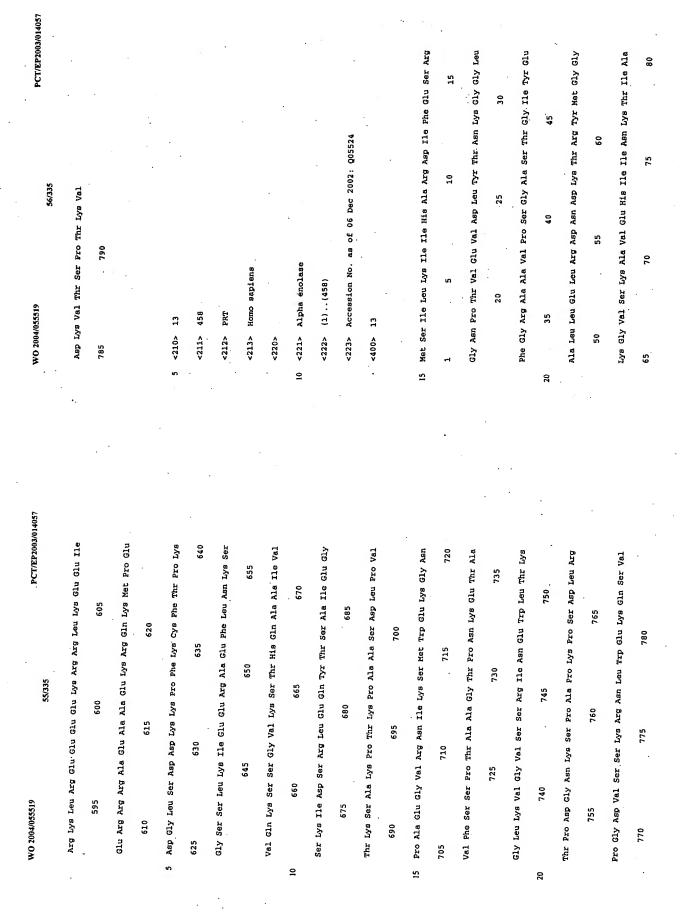
WO 2004/053519	45/335	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057
Lys Phe Ala Asp Gln His Val Pro Gly Ser Pro Phe	Pro Gly Ser Pro Phe	Ser Val Lys	Val Gln Glu Pro Gly Asp Tyr	Glu val Ser Val Lys Phe Asn Glu
2120 2125	2130		2300 2305	2310
Val Thr Gly Glu Gly Arg Val Lys Glu Ser Ile Thr	Lys Glu Ser Ile Thr	Arg Arg	Glu His Ile Pro Asp Ser Pro	Glu His Ile Pro Asp Ser Pro Phe Val Val Pro Val Ala Ser Pro
2135 2140	2145		2315 2320	2325
5 Arg Ala Pro Ser Val Ala Asn Val Gly Ser His Cys	Val Gly Ser His Cys	Asp Leu Ser	5 Ser Gly Asp Ala Arg Arg Leu	Ser Gly Asp Ala Arg Leu Thr Val Ser Ser Leu Gln Glu Ser
2150 2155	2160		2330 2335	2340
Leu Lys Ile Pro Glu Ile Ser Ile Gln Asp Met Thr	Ile Gln Asp Met Thr	Ala Gln Val	Gly Leu Lys Val Asn Gln Pro Ala Ser Phe Ala Val	Ala Ser Phe Ala Val Ser Leu Asn
2165 2170	2175		2345 . 2350	2355
Thr Ser Pro Ser Gly Lys Thr His Glu Ala Glu Ile	His Glu Ala Glu Ile	Val Glu Gly	Gly Ala Lys Gly Ala Ile Asp	Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His Ser Fro Ser Gly
10 2180 2185	2190		10 2360 2365	2370
Glu Asn His Thr Tyr Cys Ile Arg Phe Val Pro Ala		Glu Met Gly		Ala Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln Asp Lys Tyr
2195 2200	. 2205		2375 . 2380	2385
Thr His Thr Val Ser Val Lys Tyr Lys Gly Gln His		Val Pro Gly	Ala Val Arg Phe Ile Pro Arg	Glu Asn Gly Val Tyr Leu Ile Asp
2210 2215	2220		2390 2395	2400
15 Ser Pro Phe Gln Phe Thr Val Gly Pro Leu Gly Glu		Gly Gly Ala	15 Val Lys Phe Asn Gly Thr His	Ile Pro Gly Ser Pro Phe Lys Ile
2225 2230	. 2235		2405 2410	. 2415
His Lys Val Arg Ala Gly Gly Pro Gly Leu Glu Arg		Ala Glu Ala	Arg Val Gly Glu Pro Gly His	Arg Val Gly Glu Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser
2240 2245	2250		2420 2425	2430
Gly Val Pro Ala Glu Phe Ser Ile Trp Thr Arg Glu		Ala Gly Ala	Ala Tyr Gly Ala Gly Leu Glu	Ala Tyr Gly Ala Gly Leu Glu Gly Gly Val Thr Gly Asn Pro Ala
20 2255 2260	2265		20 2435 2440	2445
Gly Gly Leu Ala Ile Ala Val Glu Gly Pro Ser Lys	Glu Gly Pro Ser Lys	Ala Glu Ile	Glu Phe Val Val Asn Thr Ser	Glu Phe Val Val Asn Thr Ser Asn Ala Gly Ala Gly Ala Leu Ser
2270 2275	2280		2450 2455	2460
Ser Phe Glu Asp Arg Lys Asp Gly Ser Cys Gly Val	Gly Ser Cys Gly Val	Ala Tyr Val	Val Thr Ile Asp Gly Pro Ser	Val Thr Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu
2285 2290	2295		2465 2470	2475

Val Thr Tyr Thr Pro Met 2485 2490 Lys Tyr Gly Gly Pro Tyr 2500 2505 Lys Val Thr Gly Pro Arg 2515 2520 Pro Gln His Gly Ala Pro Arg 2535 Pro Gln His Gly Ala Pro Arg 2536 Fro Gln His Gly Ala Pro Arg 2550 Fal Val Ala Lys Gly Leu 2550 Fal Val Ala Lys Gly Leu 2550 Fau Leu Val Gly Val His Gl 2595 Fau Leu Val Gly Val His Gl 2595 Fau Val Lys His Val Gly Glu Gl 2610 Fau Lys Asp Lys Gly Glu Gl 2625 Fau His Ile Pro Gly Ser E 2625 Lu His Ile Pro Gly Ser E 2640	PCT/EP2003/014057 WO 2004/055519 48/335	Ala Pro Gly		His Ile Gly <210> 10	<211> 199	Leu Val Ser 5 <212> PRT	<213> Homo sapiens	Ser Leu <220>	<221> Transgelin 2	Gly Pro Gly <222> (1)(199)	10 <223> Accession No. as of 05 Dec 2002; P37802	Gly Leu Ser <400> 10	Asp Cys Ser	1 5 10	Gly Pro Arg	20 25 30	Ser Ang Leu Trp Ile Thr Thr Gln Cys Arg Lys Asp Val Gly Arg Pro Gln Pro Gly	35 40 45	Tyr Thr Leu	20 50 55 60	Pro Tyr Arg	. 65 . 70 . 75
2 4 5 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	47/335	Cys Pro Glu Gly Tyr Arg Val Thr Tyr Thr Pro Met Ala Pro Gly	2485 2490	Ser Tyr Leu Ile Ser Ile Lys Tyr Gly Gly Pro Tyr Hi	2500 2505	Gly Ser Pro Phe Lys Ala Lys Val Thr Gly Pro Arg Le		Asn His Ser Leu His Glu Thr Ser Ser Val Phe Val As	2530 2535	Thr Lys Ala Thr Cys Ala Pro Gln His Gly Ala Pro	2545 2550	Pro Ala Asp Ala Ser Lys Val Val Ala Lys Gly Leu	Lys Ala Tyr Val Gly Gln Lys Ser Ser Phe Thr Val	2575 2580	Lys Ala Gly Asn Asn Met Leu Leu Val Gly Val His Gl	2590 2595	Thr Pro Cys Glu Glu Ile Leu Val Lys His Val Gly	2605 2610	Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu	2620 2625	Val Val Lys Trp Gly His Glu His Ile Pro Gly Ser	2635 2640

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Leu Gln Ala Ala Gl	Leu Gin Ala Ala Glu Arg Tyr Gly Ile Asn Thr Thr Asp	Thr Asp Ile Phe Gln			<400> 11	
. 100	. 301	ç				
	3	2				
Thr Val Asp Leu Tr	Thr Val Asp Leu Trp Glu Gly Lys Asn Met Ala Cys Val Gln Arg	Cys Val Gln Arg Thr			Met Ala Gly Leu Asn Ser Leu Glu Ala Val Lys Arg Lys Ile Gln Ala	Gln Ala
115	120	125			1 . 5	15
5 Leu Met Asn Leu Gl	Leu Met Asn Leu Gly Gly Leu Ala Val Ala Arg Asp Asp Gly Leu Phe	Asp Asp Gly Leu Phe		u ,	5 Leu Gin Gin Ala Asp Glu Ala Glu Asp Arg Ala Gin Gly Leu Gin	Leu Gln
130	135	140			20 25 30	
Ser Gly Asp Pro As	Ser Gly Asp Pro Asn Trp Phe Pro Lys Lys Ser Lys Glu Asn Pro Arg	Lys Glu Asn Pro Arg		·.	Arg Glu Leu Asp Gly Glu Arg Glu Arg Glu Lys Ala Glu Gly Asp	Gly Asp
145	150 155	160			35 40 45	
Asn Phe Ser Asp As	Asn Phe Ser Asp Asn Gln Leu Gln Glu Gly Lys Asn Val Ile Gly Leu	Asn Val Ile Gly Leu			Val Ala Ala Leu Asn Arg Arg Ile Gin Leu Val Glu Glu Glu Leu Asp	Leu Asp
10 165	. 170	175		01	50 55 60	
Gln Met Gly Thr As	Gln Met Gly Thr Asn Arg Gly Ala Ser Gln Ala Gly Met	Gly Met Thr Gly Tyr			Ary Ala Gin Giu Ary Leu Ala Thr Ala Leu Gin Lys Leu Giu Giu Ala	Glu Ala
180	.185	190	· .		65 70 75	08
Gly Met Pro Arg Gln Ile Leu	n ile beu				Glu Lys Ala Ala Asp Glu Ser Glu Arg Gly Met Lys Val Ile Glu Asn	Glu Asn
195					6 06	95
15				15 '	. Arg Ala Met Lys Asp Glu Glu Lys Met Glu Ile Gln Glu Met Gln Leu	Gln Leu
					100 105	
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20 <213> Homo sapiens				20	130 135 140	
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<222> (1)(248)					Leu Lys Asn Val Thr Asn Asn Leu Lys Ser Leu Glu Ala Ala Ser Glu	Ser Glu
<223> Accession No. P07226	lo. P07226				165 170 1.	175

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51/335	27335
Lys Tyr Ser Glu Lys Glu Asp Lys Tyr Glu Glu Glu Ile Lys Leu Leu	Glu Met Arg Leu Glu Ala Glu Arg Ile Ala Tyr Gln Arg Asn Asp Asp
180 . 185 190	20 25 30
Ser Asp Lys Leu Lys Glu Ala Glu Thr Arg Ala Glu Phe Ala Glu Arg	Asp Glu Glu Glu Ala Ala Arg Glu Arg Arg Arg Arg Ala Arg Gln Glu
195 200 205	35 40 45
5 Thr Val Ala Lys Leu Glu Lys Thr Ile Asp Asp Leu Glu Glu Lys Leu	5 Arg Leu Arg Gln Lys Gln Glu Glu Ger Leu Gly Gln Val Thr Asp
210 . 215 . 220	09 25 05 .
Ala Gin Ala Lye Giu Giu Asn Val Gly Leu His Gin Thr Leu Asp Gin	Gin Val Glu Val Aen Ala Gin Asn Ser Val Pro Asp Glu Glu Ala Lys
225 230 235 240	65 70 75 80
Thr Leu Asn Glu Leu Asn Cys Ile	The The The Asn The Gln Val Glu Gly Asp Asp Glu Als Als Phe
10 245	10 85 90 95
	heu Glu Arg Leu Ala Arg Arg Glu Glu Arg Arg Gln Lys Arg Leu Gln
	100 105 110
<210> 12	Glu Ala Leu Glu Arg Gln Lys Glu Phe Asp Fro Thr 11e Thr Asp Ala
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15 <212> PRT	15 Ser Leu Ser Leu Pro Ser Arg Arg Met Gln Asn Asp Thr Ala Glu Asn
<213> Homo sapiens	130 135 140.
<220>	Glu Thr Thr Glu Lys Glu Lys Ser Glu Ser Arg Gln Glu Arg Tyr
<221> Caldesmon	145 150 155 160
<222> (1)(793)	Glu Ile Glu Glu Thr Glu Thr Val Thr Lys Ser Tyr Gln Lys Asn Asp
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	180 185 190
Met Asp Asp Phe Glu Arg Arg Arg Glu Leu Arg Arg Gln Lys Arg Glu	Glu Glu Glu Glu Lys Pro Lys Arg Gly Ser Ile Gly Glu Asn Gln Val
1 5 10 . 15	195 200 205

WO 2004/055519 54/335 FCT/EP2003/014057	Glu Thr Lys lie Lys Gly Glu Lys Val Glu Gln Lys lle Glu Gly Lys	405 410 415	Trp Val Aen Glu Lye Lye Ala Glu Glu Aep Lys beu Gln Thr Ala Vel	420 425 430	5 Leu Lys Lys Gln Gly Glu Glu Lys Gly Thr Lys Val Gln Ala Lys Arg	435 440 445	Glu Lys Leu Gln Glu Asp Lys Pro Thr Phe Lys Lys Glu Glu Ile Lys	450 455 460	Asp Glu Lys 11e Lys Lys Asp Lys Glu Pro Lys Glu Glu Val Lys Ser	10 465 470 475 480	Phe Met Asp Arg Lys Lys Gly Phe Thr Glu Val Lys Ser Gln Asn Gly	485 490 495	Glu Phe Met Thr His Lys Leu Lys His Thr Glu Asn Thr Phe Ser Arg	500 505 510	15 Pro Gly Gly Arg Ala Ser Val Asp Thr Lys Glu Ala Glu Gly Ala Pro	515 520 525	. Gln Val Glu Ala Gly Lys Arg Leu Glu Glu Leu Arg Arg Arg Arg Gly	530 535 540	Glu Thr Glu Ser Glu Glu Phe Glu Lys Leu Lys Glu Lys Glu Glu	20 545 550 555	Ala Ala Leu Glu Leu Glu Glu Leu Lys Lys Lys Arg Glu Glu Arg Arg	565 570 575	Lys Vel Leu Glu Glu Glu Glu Gln Arg Arg Lys Gln Glu Glu Ala Asp	989 285 286
WO 2004/055519 53/335 PCT/EP2003/014057	Glu Val Met Val Glu Glu Lys Thr Glu Ser Gln Glu Glu Thr Val	210 215 220	Val Met Ser Leu Lys Asn Gly Gln Ile Ser Ser Glu Glu Pro Lys Gln .	225 230 235 240	5 Glu Glu Glu Arg Glu Gln Gly Ser Asp Glu Ile Ser His His Glu Lys	245 250 255	Met Glu Glu Glu Asp Lys Glu Arg Ala Glu Ala Glu Arg Ala Arg Leu	260 265 270	Glu Ala Glu Glu Arg Ile Lys Ala Glu Gln Asp Lys Lys Ile	10 275 280 285	Ala Asp Glu Arg Ala Arg Ile Glu Ala Glu Glu Lys Ala Ala Ala Gln	290 295 300	Glu Arg Glu Arg Arg Glu Ala Glu Glu Arg Glu'Arg Met Arg Glu Glu	305 310 315 320	15 Glu Lys Arg Ala Ala Glu Glu Arg Gln Arg Ile Lys Glu Glu Glu Lys	325 330 335	Arg Ala Ala Glu Glu Arg Gln Arg Ile Lys Glu Glu Glu Lys Arg Ala	. 340 345 . 350	Ala Glu Glu Arg Gln Arg Ile Lys Glu Glu Glu Lys Arg Ala Ala Glu	20 355 360 365	Glu Arg Gln Arg Ala Arg Ala Glu Glu Glu Glu Lys Ala Lys Val Glu	370 375 380	Glu Gln Lys Arg Asn Lys Gln Leu Glu Glu Lys Lys Arg Ala Met Gln	385 390 395 400



Properties Pro		
12 25 25 25 25 25 25 25	57/335	
100 105	Pro Ala Leu Ile Ser Lys Asn Val Asn Val Glu Glu Gln Asp Lys Ile	Pro Asp Asp Pro Ser Arg Tyr Ile Ser Pro Asp Gln Leu Ala Asp Leu
100 100	06	280
190 Hay han hal life ieu Giy yel Sor Jeu Alla Wal Cye Ser Ama Ala 115 110 110 110 110 Giy Yel Sor Jeu Ala Wal Cye Ser Ama Ala 118 119 120 110 110 Giy Yel For Jeu Yor Any He Ile Ala App 119 110 110 110 Giy Yel For Jeu Yor Any He Ile Ala App 110 110 110 110 Giy Yel For Jeu Yel For Jeu Yor Any He Ile Ala App 110 110 110 110 Giy Yel For Jeu Yor Any He Ile Ala App 110 110 110 110 Giy Ala App Ary For Jeu Ala Man Ama Ama Ala Giy Ama Ana Gir Giy Ana Ana Gir Giy Ana Ana Gir Giy Ana Ana Ang Ary For Jeu Ana Ang Ary For Ang Ary For Ang Ary For Ang Ary Ang Ary For Ang Ary For Ang Ary Ang Ary For Ang Ary Ang Ary For Ang Ary For Ang Ary For Ang Ary Ang Ar	Asp Asn Leu Met Leu Asp Met Asp Gly Ser Glu Asn Lys Ser Lys Phe	Tyr Lys Gly Phe Val Leu Gly His Ala Val Lys Asn Tyr Pro Val Gly
115 120 120 125 120 125 120 125 120 125 120	105	. 295.
113 115 116 116 117 118		
130 133 135 130 133 130	120	310 315
130 135 130 135 130	Gly Ala Thr Ala Glu Lys Gly Val Pro Leu Tyr Arg His Ile Ala Asp	Lys Lys Leu Phe Thr Gly Ser Leu Val Gly Ile Gln Val Val Gly Abp
145 186 Man Ann Peo Glu Val Ite Law Peo Val Peo Val Peo Val Peo Ala Phe Ann 146 186 186 186 186 186 186 186 186 186 18	135	330
143 150	Leu Ala Gly Asn Asn Pro Glu Val Ile Leu Pro Val Pro Ala Phe Asn	Asp Leu Thr Val Thr Lys Pro Glu Ala Arg Ile Ala Lys Ala Val Glu
11 11 12 12 12 12 12 12	145 150 155	340 345
156 170 175 185	Val Ile Asn Gly Gly Ser His Ala Gly Asn Lys Leu Ala Met Gln Glu	Glu Val Lys Ala Cys Asn Cys Leu Leu Leu Lys Val Asn Gln Ile
How the tite pro Pro Cys Git Alia hap Arg Pie Ann Anp Ala lie Arg 180 180 180 180 180 180 180 18	170	360
130 131 130 131 130	Phe Met Ile Pro Pro Cys Gly Ala Asp Arg Phe Asn Asp Ala Ile Arg	Gly Ser Val Thr Glu Ser Leu Gln Ala Cys Lys Leu Ala Gln Ser Asn
136 14 15 16 14 15 15 15 15 15 15 15	185	375
195		
Tyr Gly Lys Asp Ala Thr Asn Val Gly Asp Glu Gly Gly Phe Ala Pro 210 220 Asn Ile Leu Glu Asn Lys Glu Ala Leu Glu Leu Leu Lys Thr Ala Ile 225 226 230 235 240 201 240 201 245 245 240 215 246 217 246 255 Ala Ser Glu Phe Tyr Arg Asp Gly Lys Tyr Asp Leu Asp Phe Asn Ser 260 270	200	390 395
Abn Ile Leu Glu Asn Lys Glu Ale Leu Glu Leu Leu Lys Thr Ale Ile 225 226 230 235 240 20 Gly Lys Ale Gly Tyr Ser Asp Lys Val Val Ile Gly Met Asp Val Ala 245 245 250 255 Ala Ser Glu Phe Tyr Arg Asp Gly Lys Tyr Asp Leu Asp Phe Asn Ser 260 265 270	Tyr Gly Lys Asp Ala Thr Asn Val Gly Asp Glu Gly Gly Phe Ala Pro	Asp Thr Phe Met Ala Asp Leu Val Val Gly Leu Cys Thr Gly Gln Ile
Asn Ile Leu Glu Asn Lys Glu Ala Leu Glu Leu Lys Thr Ala Ile 225 230 235 240 206 Gly Lys Ala Gly Tyr Ser Asp Lys Val Val Ile Gly Met Asp Val Ala 245 245 255 Ala Ser Glu Phe Tyr Arg Asp Gly Lys Tyr Asp Leu Asp Phe Asn Ser 260 265 270	215	410
225 240 201	Asn ile Leu Glu Asn Lys Glu Ala Leu Glu Leu Lys Thr Ala ile	Lys Thr Gly Pro Thr Cys Arg Ser Glu Arg Leu Ala Lys Tyr Asn Gln
	225 230 235	. 420 425 .
435 440 Gly Arg Aen Phe Arg Asn Pro Arg Ile Asn 450 455	Gly Lys Ala Gly Tyr Ser Asp Lys Val Val Ile Gly Met Asp Val Ala	Leu Leu Arg Ile Glu Glu Ala Glu Ala Gly Ser Lys Ala Arg Phe Ala
	245 250	440
265 270 450	Ala Ser Glu Phe Tyr Arg Asp Gly Lys Tyr Asp Leu Asp Phe Asn Ser	Gly Arg Aen Phe Arg Asn Pro Arg Ile Asn
	265	

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			60/335	
			Glu Ala Phe Lys Asp Ser Glu Gly Tyr Ile Tyr Ala Arg Gly Ala Gln	Gln
			100 105 110	
	<210> 14		Asp Met Lys Cys Val Ser Ile Gln Tyr Leu Glu Ala Val Arg Arg Leu	ren
	<211> 408		115 120 125	
	5 <212> PRT		5 Lys Val Glu Gly His Arg Phe Pro Arg Thr Ile His Met Thr Phe Val	Val
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	<220>		Pro Asp Glu Glu Val Gly Gly His Gln Gly Met Glu Leu Phe Val Gln	Gln
	<221> Aminoacylase-1		145 150 155 160	160
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			180 185 190	
	Met Thr Ser Lys Gly Pro Glu Glu Glu His Pro Ser Val	ero Ser Val Thr Leu Phe	Pro Trp Trp Val Arg Val Thr Ser Thr Gly Arg Pro Gly His Ala Ser	Ser
	1 5 10	15 .	200 205	
15	Arg Gin Tyr Leu Arg Ile Arg Thr Val Gin Pro Lys Pro Asp Tyr Gly	Pro Lys Pro Asp Tyr Gly	15 Arg Phe Met Glu Asp Thr Ala Ala Glu Lys Leu His Lys Val Val Asn	Asn
	20 25	30	210 215 220	
	Ala Ala Val Ala Phe Phe Glu Glu Thr Ala Arg Gln Leu	rg Gln Leu Gly Leu Gly	Ser ile Leu Ala Phe Arg Glu Lys Glu Trp Gln Arg Leu Gln Ser Asn	Asn
	35 40		225 230 235 240	240
	Cys Gln Lys Val Glu Val Ala Pro Gly Tyr Val Val Thr Val	al Val Thr Val Leu Thr	Pro His Leu Lys Glu Gly Ser Val Thr Ser Val Asn Leu Thr Lys Leu	nen
20	50 55	09	20 245 250 255	
	Trp Pro Gly Thr Asn Pro Thr Leu Ser Ser Ile Leu Leu	le Leu Leu Asn Ser His	Glu Gly Gly Val Ala Tyr Asn Val Ile Pro Ala Thr Met Ser Ala Ser	jer.
	70 70 70	75 80	260 . 265 270 .	
	Thr Amp Val Val Pro Val Phe Lym Glu Him Trp Ser Him	rp Ser His Asp Pro Phe	Phe Asp Phe Arg Val Ala Pro Asp Val Asp Phe Lys Ala Phe Glu Glu	11a
	85 90	56	275 280 285	

WO 2004/055519 62/335 62/335	<222> (1)(277)	<223> Accession No. as of 06 Dec 2002: P47756	<400> 15		5 Met Ser Asp Gln Gln Leu Asp Cys Ala Leu Asp Leu Met Arg Arg Leu	1 5 10 15	Pro Pro Gln Gln Ile Glu Lys Asn Leu Ser Asp Leu Ile Asp Leu Val	. 20 25 30	Pro Ser Leu Cys Glu Asp Leu Leu Ser Val Asp Gln Pro Leu Lys	10 35 40 45	Ile Ala Arg Asp Lys Val Val Gly Lys Asp Tyr Leu Leu Cys Asp Tyr	50 55 60	Asn Arg Asp Gly Asp Ser Tyr Arg Ser Pro Trp Ser Asn Lys Tyr Asp	65 70 75 80	15 Pro Pro Leu Glu Asp Gly Ala Met Pro Ser Ala Arg Leu Arg Lys Leu		Glu Val Glu Ala Asn Asn Ala Phe Asp Gln Tyr Arg Asp Leu Tyr Phe	100 105 110	Glu Gly Gly Val Ser Ser Val Tyr Leu Trp App Leu Asp His Gly Phe	20 115 120 125	Ala Gly Val Ila Lau Ila Lys Lys Ala Gly Asp Gly Ser Lys Lys Ile	130 135 140	Lys Gly Cys Trp Asp Ser Ile His Val Val Glu Val Glu Lys Ser	145 150 155 160		
WO 2004/055519 PCT/RP2003/014057 61/335	Gln Leu Gln Ser Trp Cys Gln Ala Ala Gly Glu Gly Val Thr Leu Glu	. 290 295 300	Phe Ala Gln Lys Trp Met His Pro Gln Val Thr Pro Thr Asp Asp Ser	305 310 315 320	5 Asn Pro Trp Ala Ala Phe Ser Arg Val Cys Lys Asp Met Asn Leu	325 330 335	Thr Leu Glu Pro Glu Ile Met Pro Ala Ala Thr Asp Asn Arg Tyr Ile	340 345 350	Arg Ala Val Gly Val Pro Ala Leu Gly Phe Ser Pro Met Asn Arg Thr	10 355 360 365	Pro Val Leu Leu His Asp His Asp Glu Arg Leu His Glu Ala Val Phe	370 375 380	Leu Arg Gly Val Asp Ile Tyr Thr Arg Leu Leu Pro Ala Leu Ala Ser	385 390 395 400	15 Val Pro Ala Leu Pro Ser Asp Ser	405			<210> 15	20 <211> 277	<212> PRT	<213> Homo septens	<220>	<221> F-actin capping protein beta subunit		

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WO 2004/055519 PCT/FP29/014/05	63/335	Ser Gly Arg Thr Ala His Tyr Lys Leu Thr Ser Thr Val Met Leu Trp	165 170 175	Leu Gln Thr Asn Lys Ser Gly Ser Gly Thr Met Asn Leu Gly Gly Ser	180 185 190	5 Leu Thr Arg Gln Met Glu Lys Asp Glu Thr Val Ser Asp Cys Ser Pro	195 200 205	His Ile Ala Asn Ile Gly Arg Leu Val Glu Asp Met Glu Asn Lys Ile	210 215 220	Arg Ser Thr Leu Asn Glu Ile Tyr Phe Gly Lys Thr Lys Asp Ile Val	10 225 230 235 240	Asn Gly Leu Arg Ser lle Asp Ala Ile Pro Asp Asn Gln Lys Phe Lys	. 245 250 255	Gln Leu Gln Arg Glu Leu Ser Gln Val Leu Thr Gln Arg Gln Ile Tyr	260 265 270	15 Ile Gln Pro Asp Asn				<210> 16	20 <211> 289	<212> PRT	<213> Homo sapiens	<220>	

WO 2004/055519	\$11/39	PCT/EP2003/014057	WO 2004/055519	PCTV	PCT/EP2003/014057
Val Asp Asp Pro Asp Ala	Val Asp Asp Pro Asp Ala Ala Asn Tyr Asn Asp Ile Asn	Asp Val Lys			
165	170	175	<221> Galectin-3 (Gal	<221> Galectin-3 (Galactose-specific lectin 3)	
Arg Leu Lys Pro Gly Tyr	Arg Leu Lys Pro Gly Tyr Leu Glu Ala Thr Val Asp Trp	Phe Arg	<222> (1)(250)	· · ·	
180	185	190	<223> Accession No. a	Accession No. as of 06 Dec 2002: P17931	
5 Tyr Lys Val Pro Asp Gly	Tyr Lys Val Pro Asp Gly Lys Pro Glu Asn Glu Phe Ala	Phe Asn Ala	5 <400> 17		
. 195	200 205				
Glu Phe Lys Asp Lys Asp	Glu Phe Lys Asp Lys Asp Phe Ala Ile Asp Ile Iys Ser Thr His	Ser Thr His	Met Ala Asp Asn Phe Se	Met Ala Asp Asn Phe Ser Leu His Asp Ala Leu Ser Gly Ser Gly Asn	ly Asn
210	215 220		is.	10 15	10
Asp His Trp Lys Ala Leu	Asp His Trp Lys Ala Leu Val Thr Lys Lys Thr Asn Gly Lys Gly Ile	Lys Gly Ile	Pro Asn Pro Gln Gly Tr	Pro Asn Pro Gln Gly Trp Pro Gly Ala Trp Gly Asn Gln Pro Ala Gly	ia Gly
10 225 230	235	240	19 . 20	25 30	
Ser Cys Met Asn Thr Thr	Ser Cys Met Asn Thr Thr Leu Ser Glu Ser Pro Phe Lys Cys Asp Pro	Сув Авр Рго	Ala Gly Gly Tyr Pro Gl	Ala Gly Gly Tyr Pro Gly Ala Ser Tyr Pro Gly Ala Tyr Pro Gly Gln	ly Gln
245	. 250	255	38	40 45 :	
Asp Ala Ala Arg Ala Ile	Asp Ala Ala Arg Ala Ile Val Asp Ala Leu Pro Pro Pro Cys Glu Ser	Cys Glu Ser	Ala Pro Pro Gly Ala Ty	Ala Pro Pro Gly Ala Tyr Pro Gly Gln Ala Pro Pro Gly Ala Tyr His	r His
260	265	270	90	60	
15 Ala Cys Thr Val Pro Thr	Ala Cys Thr Val Pro Thr Asp Val Asp. Lys Trp Phe His His Gln Lys	His Gln Lys	15 Gly Ala Pro Gly Ala Ty	Gly Ala Pro Gly Ala Tyr Pro Gly Ala Pro Ala Pro Gly Val Tyr Pro	T Pro
. 275	280 285		65 70	. 75	88 .
. Авп			Gly Pro Pro Ser Gly Pr	Gly Pro Pro Ser Gly Pro Gly Ala Tyr Pro Ser Ser Gly Gln Pro Ser	to Ser
				95	
			Ala Pro Gly Ala Tyr Pr	Ala Pro Gly Ala Tyr Pro Ala Thr Gly Pro Tyr Gly Ala Pro Ala Gly	a 61y
			20 . 100	105 110	
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<211> 250			115	120 125	
<212> PRT			Arg Met Leu Ile Thr Il	Arg Met Leu Ile Thr Ile Leu Gly Thr Val Lys Pro Asn Ala Asn Arg	n Arg
<213> Homo sapiens			130	135 . 140	

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	WO 2004/055519 PCT/EP2003/014057 67/335	WO 2004/055519 PCT/EP2003/014057 68/335	
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	165 170 175	1 5 10 15	
	5 Leu Asp Asn Asn Trp Gly Arg Glu Glu Arg Gln Ser Val Phe Pro Phe	5 Ile Gly Arg Gly Leu Glu Ser His Ile Thr Met Cys Ile Pro Pro Ser	
	180 185 190	20 25 30	
	Glu Ser Gly Lys Pro Phe Lys Ile Gln Val Leu Val Glu Pro Asp His	Tyr Ala Asp Leu Gly Lys Ala Ala Arg Asp Ile Phe Asn Lys Gly Phe	
	195 . 200 205	35 40 45	
	Phe Lys Val Ala Val Asn Asp Ala His Leu Cln Tyr Asn His Arg	Gly Phe Gly Leu Val Lys Leu Asp Val Lys Thr Lys Ser Cys Ser Gly	
	10 210 215 220	10 50 55 60	
	Val Lys Lys Leu Asn Glu Ile Ser Lys Leu Gly Ile Ser Gly Asp Ile	Val Glu Phe Ser Thr Ser Gly Ser Ser Asn Thr Asp Thr Gly Lys Val	
	225 230 235 240	65 70 75 80	
	Asp Leu Thr Ser Ala Ser Tyr Thr Met Ile	Thr Gly Thr Leu Glu Thr Lys Tyr Lys Trp Cys Glu Tyr Gly Leu Thr	
	245 250	56 06 58	
	15	15 Phe Thr Glu Lya Trp Asn Thr Asp Asn Thr Leu Gly Thr Glu Ile Ala	
		100 105 110	
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	20 <213> Homo sapiens	20 130 135 140	
	<220>	Lys Arg Glu Cys Ile Asn Leu Gly Cys Asp Val Asp Phe Asp Phe Ala	
	<221> Voltage-dependent anion-selective channel protein 2 (VDAC-2)	145 150 155 160	
	<222> (1)(347)	Gly Pro Ala 11e His Gly Ser Ala Val Phe Gly Tyr Glu Gly Trp Leu	
	<223> Accession No.as of 06 Dec 2002: P45880	165 170 175	
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	WO 2004/055519	PCT/EP2003/014057	. WO 2004/055519 PCT/EP2003/014057	/014057
	69/335	-	70/335	
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	195 200	205	<213> Homo sapiens	
ĸ	Asn Val Asn Asp Gly Thr Glu Phe Gly Gly Ser Ile Tyr Gln Lys Val	ile Tyr Gin Lys Val	5 <220>	
	210 215		<221> Annexin II	
	Cys Glu Asp Leu Asp Thr Ser Val Asn Leu Ala Trp Thr Ser Gly Thr	Trp Thr Ser Gly Thr	<222> (1)(339)	
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	Ala Ser Ile Ser Ala Lys Val Asn Asn Ser Ser Leu Il	Leu ile Gly Val Gly	Met Ser Thr Val His Glu Ile Leu Cys Lys Leu Ser Leu Glu Gly Asp	
	260 265	270	. 1 5 10 15	
	Tyr Thr Gln Thr Leu Arg Pro Gly Val Lys Leu Thr Leu Ser Ale Leu	Thr Leu Ser Ale Leu	His Ser Thr Pro Pro Ser Ala Tyr Gly Ser Val Lys Ala Tyr Thr Asn	
	275 280		. 25 30	
15	Val Asp Gly Lys Ser Ile Asn Ala Gly Gly His Lys Val Gly Ser Pro	ьув Val Gly Ser Pro	15 Phe Asp Ala Glu Arg Asp Ala Leu Asn Ile Glu Thr Ala Ile Lys Thr	
	290 295	300	35 40 45	
	Trp Ser Trp Arg Leu Asn Pro Ala Glu Arg Asn Leu Tr	teu Trp Glu Trp Ile	Lys Gly Val Asp Glu Val Thr 11e Val Asn 11e Leu Thr Asn Arg Ser	
	305 310 315	320	. 55 60 .	
	Ser Glu Asp Leu Ala Leu Ile Tyr Phe His Cys Asp Gln Gln Gln Ala	aep Gln Gln Ala	Asn Ala Gin Arg Gin Asp Ile Ala Phe Ala Tyr Gin Arg Arg Thr Lys	
2	325 330	335	20 65 70 75 80	
	Phe Phe Pro Pro Glu Asp Asp Gln Asn Lys Gly		Lys Glu Leu Ala Ser Ala Leu Lys Ser Ala Leu Ser Gly His Leu Glu	
	340 345		. 85	•
			Thr Val Ile Leu Gly Leu Leu Lys Thr Pro Ala Gln Tyr Asp Ala Ser	•

WO 2004/055519	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057
		72/335	
Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu	Glu Asp Ser Leu	Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr Tyr Ile Gln	r Ile Gln
115 120	125	305 310 315	320
ile Glu ile ile Cys Ser Arg Thr Asn Gln Glu Leu Gln	ı Gin Glu ile Asn	Gln Asp Thr Lys Gly Asp Tyr Gln Lys Ala Leu Leu Tyr Leu Cys Gly	n Cys Gly
130 135 140		325 330	335
Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys	Lys Asp Ile Ile	5 Gly Asp Asp	
145 . 150 155	160		
Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala	Ala Leu Ala Lys		
165 170	175		
Gly Arg Arg Ala Glu Asp Gly Ser Val Ile Asp Tyr Glu	Glu Leu Ile Asp	<210> 20	
180 185	190	10 <211> 418	
Gln Asp Ale Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr	Arg Lys Gly Thr	<212> PRT .	
. 200	205	<213> Homo sapiens	
Asp Val Pro Lys Trp lle Ser Ile Met Thr Glu Arg Ser Val Pro His	Ser Val Pro His	<220>	
210 215 220		<221> Collagen-binding protein 2 precursor	
Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met	Pro Tyr Asp Met	15 <222> (1)(418)	
225 230 235	240	<223> Accession No. as of 06 Dec 2002: P50454	٠.
Leu Glu Ser Ile Arg Lys Glu Vel Lys Gly Asp Leu Glu Asn Ala Phe	Glu Asn Ala Phe	<400> 20	
. 245 250 .	255		
Leu Asn Leu Val Gin Cys Ile Gin Asn Lys Pro Leu Tyr Phe Ala Asp	Tyr Phe Ala Asp	Met Arg Ser Leu Leu Leu Ser Ala Phe Cys Leu Leu Glu Ala Ala	Ala Ala
260 265	270	20 1 5 10	. 15
Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp	Asp Lys Val Leu	Leu Ala Ala Glu Val Lys Lys Pro Ala Ala Ala Ala Ala Pro Gly Thr	Gly Thr
275 280 2	285	20 25 30	
lle Arg lle Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg	Leu Lys lle Arg	Ala Glu Lys Leu Ser Pro Lys Ala Ala Thr Leu Ala Glu Arg Ser Ala	Ser Ala
290 295 300		35 40 45	

	WO 2004/055519	PCT/	PCT/RP2003/014057	WO 2004/055519	PCT/EP2003/014057
	Gly Leu Ala Phe Ser Leu Tyr Gln Ala Met Ala Lys Asp	Ala Met Ala Lys Asp Gln Ala Val	a Val	Gly Leu fyr Asn fyr fyr Asp Asp	Gly Leu Tyr Asn Tyr Tyr Asp Asp Glu Lys Glu Lys Leu Gln Ile Val
	50 55	09		245	250 255
	Glu Asn Ile Leu Val Ser Pro Val Val Val Ala Ser Ser	Val Val Ala Ser Ser Leu Gly Leu	y Leu	Glu Met Pro Leu Ala His Lys Leu	Glu Met Pro Leu Ala His Lys Leu Ser Ser Leu Ile Ile Leu Met Pro
	. 70	. 75	98	260	265 270
'n	Val Ser Leu Gly Gly Lys Ala Thr Thr Ala Ser Gln Ala	Thr Ala Ser Gln Ala Lys Ala Val		5 His His Val Glu Pro Leu Glu Arg	His His Val Glu Pro Leu Glu Arg Leu Glu Lys Leu Leu Thr Lys Glu
	85	96		275 280	285
	Leu Ser Ala Glu Gln Leu Arg Asp Glu Glu Val His Ala	Glu Glu Val His Ala Gly Leu Gly	n Gly	Gln Leu Lys Ile Trp Met Gly Lys	Gln Leu Lys Ile Trp Met Gly Lys Met Gln Lys Lys Ala Val Ala Ile
	100	105		290 295	300
	Glu Leu Leu Arg Ser Leu Ser Asn Ser Thr Ala Arg Asn	Ser Thr Ala Arg Asn Val Thr	עבל זו	Ser Leu Pro Lys Gly Val Val Glu	Ser Leu Pro Lys Gly Val Val Glu Val Thr His Asp Leu Gin Lys His
10	115 120	125		10 305 . 310	320
	Lys Leu Gly Ser Arg Leu Tyr Gly Pro Ser Ser Val Ser	Pro Ser Ser Val Ser Phe Ala Asp	а Авр.	Leu Ala Gly Leu Gly Leu Thr Glu	Leu Ala Gly Leu Gly Leu Thr Glu Ala Ile Asp Lys Asn Lys Ala Asp
	130 135	140		325	330 335
	Asp Phe Val Arg Ser Ser Lys Gln His Tyr Asn Cys Glu	His Tyr Asn Cys Glu His Ser Lys	r Lys	Leu Ser Arg Met Ser Gly Lys Lys	Leu Ser Arg Het Ser Gly Lys Lys Asp Leu Tyr Leu Ala Ser Val Phe
	145 150	155		340	345 350
15	ile Aen Phe Arg Aep Lys Arg Ser Ala Leu Gln Ser Ile	Ala Leu Gln Ser Ile Asn Glu Trp		15 His Ala Thr Ala Phe Glu Leu Asp	His Ala Thr Ala Phe Glu Leu Asp Thr Asp Gly Asn Pro Phe Asp Gln
	165	170 . 175		355 360	365
	Ala Ala Gln Thr Thr Asp Gly Lys Leu Pro Glu Val Thr	Leu Pro Glu Val Thr Lys Asp Val	p Val	Asp Ile Tyr Gly Arg Glu Glu Leu	Asp ile Tyr Gly Arg Glu Glu Leu Arg Ser Pro Lys Leu Phe Tyr Ala
	180	185		370 375	. 380
	Glu Arg Thr Asp Gly Ala Leu Leu Val Asn Ala Met Phe	Val Asn Ala Met Phe Phe Lys Pro	s Pro	Asp His Pro Phe Ile Phe Leu Val	Asp His Pro Phe Ile Phe Leu Val Arg Asp Thr Gln Ser Gly Ser Leu
20	195 200	205.		20 385 390	395 400
	His Trp Asp Glu Lys Phe His His Lys Met Val Asp Asn	Lys Met Val Asp Asn Arg Gly Phe	y Phe	Leu Phe Ile Gly Arg Leu Val Arg	Leu Phe Ile Gly Arg Leu Val Arg Pro Lye Gly Asp Lye Met Arg Asp
	210 215	220		405	410 415
	Met Val Thr Arg Ser Tyr Thr Val Gly Val Met Met Met	Gly Val Met Met Met His Arg Thr	g Thr	Glu Leu	
	225 . 230	235	240		

	WO 2004/055519		75/335	PCT/EP2003/014057		WO 2004/055519	76/335		PCT/EP2003/014057
						Glu Asp Leu Val F	Glu Asp Leu Val Phe Ile Phe Trp Ala Pro Glu Ser Ala Pro Leu Lys	Glu Ser Ala F	ro Leu Lys
						100	501	н	110
	<210> 21					Ser Lys Met Ile T	Ser Lye Met Ile Tyr Ala Ser Ser Lye Asp Ala Ile Lye Lye Leu	Ala Ile Lys L	ув Гув Гец
	<211> 166					115	. 120	125	
'n	<212> PRT				¥n.		Thr Gly 11e Lys His Glu Leu Gln Ala Asn Cys Tyr Glu Glu Val Lys	Cys Tyr Glu.G	lu Val Lys
	<213> Homo	Homo sapiens		•		130	135	140	
	<220>					Asp Arg Cys Thr L	Asp Arg Cys Thr Leu Ala Glu Lys Leu Gly Gly Ser Ala Val Ile Ser	Gly Ser Ala V	al Ile Ser
	<221> Cof1	Cofilin, non-muscle isoform	oform			145	150	155	160
	<222> (1)	(1)(166)				jeu Glu Gly Lys Pro Leu	ro Leu		
9		<223> Accession No. as of 08 ec 2002; P23528	ec 2002: P23528		10	मं	165		
	<400> 21								
	Met Ala Ser	Gly Val Ala Val Se	Met Ala Ser Gly Val Ala Val Ser Asp Gly Val Ile Lys	rs Val Phe Asn		<210> 22			
	ਜ	ភ	10	15		<211> 165			
15		Val Arg Lys Ser Se	Asp Met Lys Val Arg Lys Ser Ser Thr Pro Glu Glu Val Lys Lys Arg	Lys Lys Arg		<212> PRT			
		20	25	30		<213> Homo sapiens			
	Lys Lys Ala	Val Leu Phe Cys Le	Lys Lys Ala Val Leu Phe Cys Leu Ser Glu Asp Lys Lys	's Asn Ile Ile	٠.	<220>			
	35	40	, 45			<221> Peptidyl-pr	<221> Peptidyl-prolyl cis-trans isomerase A	8e A	
•	Leu Glu Glu	Gly Lys Glu Ile Le	Leu. Glu Glu Lys Glu Ile Leu Val Gly Asp Val Gly Gln Thr Val	Gln Thr Val		<222> (1) .: (165)			
20	20	55	09		20	<223> Accession N	Accession No. as of 09 Dec 2002; P05092	P05092	
	Asp Asp Pro	Tyr Ala Thr Phe Va	Asp Asp Pro Tyr Ala Thr Phe Val Lys Met Leu Pro Asp Lys Asp Cys	Lys Asp Cys		<400> 22	٠.		
	. 29	70	. 57	80					
	Arg Tyr Ala	Leu Tyr Asp Ala Th	Arg Tyr Ala Leu Tyr Asp Ala Thr Tyr Glu Thr Lys Glu Ser Lys Lys	Ser Lys Lys		Met Val Asn Pro Th	Met Val Asn Pro Thr Val Phe Phe Asp Ile Ala Val Asp Gly Glu Pro	ala val Asp Gl	y Glu Pro
		85	96	95		1 5	.10		15

WO 2004/055519	PCT/EP2003/014057	WO 2004/055519 78/335	PCT/EP2003/014057
Leu Gly Arg Val Ser Phe Glu Leu Phe Ala Asp Lys Val	he Ala Asp Lys Val Pro Lys Thr		
20	25 30	<213> Homo sapiens	
Ala Glu Asn Phe Arg Ala Leu Ser Thr Gly Glu Lys Gly	hr Gly Glu Lys Gly Phe Gly Tyr	<220>	
35 40	45	<221> Dynein intermediate chain 2, cytosolic	сутовојіс
5 Lys Gly Ser Cys Phe His Arg Ile Ile Pro Gly Phe Met	le Pro Gly Phe Met Cys Gln Gly	5 <222> (1) (638)	
. 50 55	. 09	<223> Accession No. as of 09 Dec 2002: Q13409	
Gly Asp Phe Thr Arg His Asn Gly Thr Gly Gly Lys Ser	hr Gly Gly Lys Ser Ile Tyr Gly	<400> 23	·
65 70	75 80		
Glu Lys Phe Glu Asp Glu Asn Phe 11e Leu Lys His Thr	le Leu Lys His Thr Gly Pro Gly	Met Ser Asp Lys Ser Glu Leu Lys Ala Glu Leu Glu Arg Lys Lys Gln	Glu Leu Glu Arg Lys Lys Gln
10 85		10 1 5	. 15
Ile Leu Ser Met Ala Agn Ala Gly Pro Asn Thr Agn Gly Ser Gln Phe	ro Asn Thr Asn Gly Ser Gln Phe	Arg Leu Ala Gln Ile Arg Glu Glu Lys Lys Arg Lys Glu Glu Glu Arg	Lys Arg Lys Glu Glu Glu Arg
100	105	20 25	30
Phe Ile Cys Thr Ala Lys Thr Glu Trp Leu Asp Gly Lys His Val Val	rp Leu Asp Gly Lys His Val Val	Lys Lys Lys Glu Thr Asp Gln Lys Lys Glu Ala Vel Ala Pro Val Gln	Glu Ala Val Ala Pro Val Gln
115 120	125	35 40	45
15 Phe Gly Lys Val Lys Glu Gly Met Asn Ile Val Glu Ala Met Glu Arg	sn ile Val Glu Ala Met Glu Arg	15 Glu Glu Ser Asp Leu Glu Lys Lys Arg Arg Glu Ala Glu Ala Leu Leu	Arg Glu Ala Glu Ala Leu
130 135	140		09
Phe Gly Ser Arg Asn Gly Lys Thr Ser Lys Lys Ile Thr Ile Ala Asp	er Lys Lys Ile Thr Ile Ala Asp	Gin Ser Met Gly Leu Thr Pro Glu Ser Pro Ile Val Phe Ser Glu Tyr	Pro Ile Val Phe Ser Glu Tyr
145 150	155 160		75 . 80
Cys Gly Gln Leu Glu		Trp Val Pro Pro Met Ser Pro Ser Ser Lys Ser Val Ser Thr Pro	Ser Lys Ser Val Ser Thr Pro
20 165	•	. 85 .	36 06
		Ser Glu Ala Gly Ser Gln Asp Ser Gly Asp Gly Ala Val Gly Sor Arg	Asp Gly Ala Val Gly Ser Arg
		100 105	110
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WO 2004/055519 79/335	PCT/EP2003/014057	WO 2004/055519
Ser Amp Leu Gly Arg Gly Pro Ile Lys Leu Gly Met Ala Lys Ile Thr	fs Leu Gly Met Ala Lys lle Thr	Lys Lys Thr Thr Pro
130 135	140	325
Gln Val Asp Phe Pro Pro Arg Glu ile Val Thr Tyr Thr Lys Glu Thr	te Val Thr Tyr Thr Lys Glu Thr	Ser Ala Thr Phe Ala
145 150	155 160	340
Gln Thr Pro Val Met Ala Gln Pro Lys Glu Asp Glu Glu Glu Asp Asp	rs Glu Asp Glu Glu Glu Asp Asp	5 Tyr Ser Gly Gln Ile
165	170 175	355
Asp Val Val Ala Pro Lys Pro Pro Ile Glu Pro Glu Glu Glu Lys Thr	e Glu Pro Glu Glu Lys Thr	Pro Val Gln Arg Thr
180 185	5 190	370
Leu Lys Lys Asp Glu Glu Asn Asp Ser Lys Ala Pro Pro His Glu Leu	r Lys Ala Pro Pro His Glu Leu	Tyr Cys Val Asn Val
195 200		10 385
Thr Glu Glu Glu Lys Gln Gln Ile Leu His Ser Glu Glu Phe Leu Ser	u His Ser Glu Glu Phe Leu Ser	Ile Ser Thr Asp Gly
210 215	220	405
Phe Phe Asp His Ser Thr Arg Ile Val Glu Arg Ala Leu Ser Glu Gln	l Glu Arg Ala Leu Ser Glu Gln	His Pro Gln Asp Ser
225 230	235 240	. 420
Ile Asn Ile Phe Phe Asp Tyr Ser Gly Arg Asp Leu Glu Asp Lys Glu	Y Arg Asp Leu Glu Asp Lys Glu	15 Ala Val Thr Ser Met
245	250 . 255	435
Gly Glu Ile Gln Ala Gly Ala Lys Leu Ser Leu Asn Arg Gln Phe Phe	u Ser Leu Asn Arg Gln Phe Phe	Val Gly Ser Glu Glu
. 260 265		450
Asp Glu Arg Trp Ser Lys His Arg Val Val Ser Cys Leu Asp Trp Ser	1 Val Ser Cys Leu Asp Trp Ser	Lys Ala Gly Ile Ser
275 280	285	20 465
Ser Gln Tyr Pro Glu Leu Leu Val Ala Ser Tyr Asn Asn Asn Glu Asp	a Ser Tyr Asn Asn Asn Glu Asp	Gly Ile His Cys His
. 295	900	485
Ala Pro His Glu Pro Asp Gly Val Ala Leu Val Trp Asn Met Lys Tyr	i Leu Val Trp Asn Met Lys Tyr	Phe Val Thr Ser Ser
305 310	. 315 320	005

Asp Gly Lys Ile Cys Ser Trp Ser Leu Asp Met Leu Ser

Asp Ser Met Glu Leu Val His Lys Gln Ser Lys Ala Val

Ser Met Ser Phe Pro Val Gly Asp Val Asn Asn Phe Val

Glu Glu Gly Ser Val Tyr Thr Ala Cys Arg His Gly Ser

Ile Ser Glu Met Phe Glu Gly His Gln Gly Pro Ile Thr

Cys His Ala Ala Val Gly Ala Val Asp Phe Ser His Leu

Ser Ser Phe Asp Trp Thr Val Lys Leu Trp Thr Thr Lys

Asn Val Val Gly Thr Gln Asn Ala His Asn Leu Ile Ser

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Thr Pro Glu Tyr Val Phe His Cys Gln Ser Ala Val Met

Phe Ala Lys Phe His Pro Asn Leu Val Val Gly Gly Thr

Gln Ile Val Leu Trp Asp Asn Arg Ser Asn Lys Arg Thr

Arg Thr Pro Leu Ser Ala Ala Ala His Thr His Pro Val

WO 2004/055519 PCT/EP2003/014057 81/335.	WO 2004/055519 PCT/EP2003/014057 82/335
Asn Asn Lys Pro Leu Tyr Ser Phe Glu Asp Asn Ala Asp Tyr Val Tyr	<222> (1)(328)
515 . 520 525	<223> Accession No. as of 09 Dec 2002: Q13011
Asp Val Met Trp Ser Pro Thr His Pro Ala Leu Phe Ala Cys Val Asp	<400> 24
530 535 540	
5 Gly Met Gly Arg Leu Asp Leu Trp Asn Leu Asn Asn Asp Thx Glu Val	5 Met Ala Ala Gly Ile Val Ala Ser Arg Arg Leu Arg Asp Leu Leu Thr
545 550 560	1 5 10 15
Pro Thr Ala Ser Ile Ser Val Glu Gly Asn Pro Ala Leu Asn'Arg Val	Arg Arg Leu Thr Gly Ser Asn Tyr Pro Gly Leu Ser Ile Ser Leu Arg
565 570 . 575	20 . 25 30
Arg Trp Thr His Ser Gly Arg Glu Ile Ala Val Gly Asp Ser Glu Gly	Leu Thr Gly Ser Ser Ala Glu Glu Ala Ser Gly Val Ala Leu Gly
00 580 585 590	10 35 40 45
Gln ile Val ile Tyr Asp Val Gly Glu Gln ile Ala Val Pro Arg Asn	Glu Ala Pro Asp His Ser Tyr Glu Ser Leu Arg Val Thr Ser Ala Gln
595 600 605	90 25 60
Asp Glu Trp Ala Arg Phe Gly Arg Thr Leu Ala Glu Ile Asn Ala Asn	Lys His Val Leu His Val Gin Leu Asn Arg Pro Asn Lys Arg Asn Ala
610 615 620	65 70 75 80
is Arg Ala Asp Ala Glu Glu Ala Ala Thr Arg Ile Pro Ala	is Met Asn Lys Val Phe Trp Arg Glu Met Val Glu Cys Phe Asn Lys Ile
625 . 630 635	85 90
	Ser Arg Asp Ala Asp Cys Arg Ala Val Val Ile Ser Gly Ala Gly Lys
	100 105 110
<210> 24	Met Phe Thr Ala Gly Ile Asp Leu Het Asp Met Ala Ser Asp Ile Leu
20 <211> 328	20 115 120 125
<212> PRT	Gin Pro Lys Gly Asp Asp Val Ala Arg Ile Ser Try Tyr Leu Arg Asp
<213> Homo sapiens	130 135 140
<220>	Ile Ile Thr Arg Tyr Gln Glu Thr Phe Asn Val Ile Glu Arg Cys Pro
<221> Deltal, 5-deltal, 4-dienoyl-CoA isomerase, mitochondrial precursor	145 150 155 160

	WO 2004/055519	PCT/EP2003/014057	WO 2004/055519	PCT/EP	PCT/EP2003/014057
	83/335			84/335	
	Lys Pro Val Ile Ala Ala Val His Gly Gly Cys Ile Gly	s Ile Gly Gly Gly Val	<210> 25		
	. 165 170	175	<211> 1657		
	Asp Leu Val Thr Ala Cys Asp Ile Arg Tyr Cys Ala Gln	Ala Gln Asp Ala Phe	<212> PRT		
	180 185	190	<213> Homo sapiens		•
••	5 Phe Gln Val Lys Glu Val Asp Val Gly Leu Ala Ala Asp	Ala Asp Val Gly Thr	5 <220>		
	195 200	205	<221> Ras GTPa	Ras GTPase-activating-like protein IQGAP1	
	Leu Glu Arg Leu Pro Lys Val Ile Gly Asn Gln Ser Leu	Ser Leu Val Asn Glu	<222> (1)(1657)	57)	
	210 215	220	<223> Accessio	Accession No. as of 09 Dec 2002; P46940	
	Leu Ala Phe Thr Ala His Lys Met Met Ala Asp Glu Ala	Glu Ala Leu Asp Ser	<400> 25		
9	225 230 235	240	01		
	Gly Leu Val Ser Arg Val Phe Pro Asp Lys Glu Val Met Leu Asp Ala	Val Met Leu Asp Ala	Met Ser Ala Ala	Met Ser Ala Ala Asp Glu Val Asp Gly Leu Gly Val Ala Arg Pro His	
	245 250	255		5 10 15	
	Ala Leu Pro Leu Ala Pro Glu Ile Ser Ser Lys Thr Thr Val Leu Val	Thr Thr Val Leu Val	Tyr Gly Ser Val	Tyr Gly Ser Val Leu Asp Asn Glu Arg Leu Thr Ala Glu Glu Met Asp	
	. 260 265	270	. 20	25 30	
15	Gin Ser Thr Lys Val Asn Leu Leu Tyr Ser Arg Asp His Ser Val Ala	Asp His Ser Val Ala	15 Glu Arg Arg Arg	Glu Arg Arg Gin Asn Val Ala Tyr Glu Tyr Leu Cys His Leu Glu	
•	275 280	285	35		•
	Glu Ser Leu Asn Tyr Val Ala Ser Trp Asn Met Ser Met	Ser Met Leu Gln Thr	Glu Ala Lys Arg	Glu Ala Lys Arg Trp Met Glu Ala Cys Leu Gly Glu Asp Leu Pro Pro	
	290 295	300	90	55 60	
	Gin Asp Leu Val Lys Ser Val Gin Pro Thr Thr Glu Asn Lys Glu Leu	Glu Asn Lys Glu Leu	Thr Thr Glu Leu	Thr Thr Glu Leu Glu Glu Gly Leu Arg Asn Gly Val Tyr Leu Ala Lys	_
20	305 310 315	320	. 20 65	70 · 75 80	
	Lys Thr Val Thr Phe Ser Lys Leu		Leu Gly Asn Phe	Leu Gly Asn Phe Phe Ser Pro Lys Val Val Ser Leu Lys Lys Ile Tyr	
	325			85 90 95	

Asp Arg Glu Gln Thr Arg Tyr Lys Ala Thr Gly Leu His Phe Arg His

	WO 2004/055519 85/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057 86/335
	Thr Asp Asn Val Ile Gin Trp Leu Asn Ala Met Asp Glu Ile Gly Leu	a Met Asp Glu Ile Gly Leu	Thr Phe Ser Ala Leu Ala Asn Ile Asp Leu Ala Leu Glu Gln Gly Asp
	115 120	125	305 310 315 320
	Pro Lys ile Phe Tyr Pro Glu Thr Thr Asp ile Tyr Asp Arg Lys Asn	p Ile Tyr Asp Arg Lys Asn	Ala Leu Ala Leu Phe Arg Ala Leu Gln Ser Pro Ala Leu Gly Leu Arg
	130 135	140	325 330 335
'n	Met Pro Arg Cys Ile Tyr Cys Ile His Ala Leu Ser Leu	a Leu Ser Leu Tyr Leu Phe	5 Gly Leu Gln Gln Gln Ber Asp Trp Tyr Leu Lys Gln Leu Leu Ser
,	145 150	155 160	340 345 350
	Lys Leu Gly Leu Ala Pro Gln Ile Gln Asp Leu Tyr Gly Lys Val Asp	p Leu Tyr Gly Lys Val Asp	Asp Lys Gln Gln Lys Arg Gln Ser Gly Gln Thr Asp Pro Leu Gln Lys
	165 170	0 175	355 360 365
	Phe Thr Glu Glu Glu Ile Asn Aan Met Lys Thr Glu Leu Glu Lys Tyr	s Thr Glu Leu Glu Lys Tyr	Glu Glu Leu Gln Ser Gly Val Asp Ala Asn Ser Ala Ala Gln Gln
2	180 185	190	10 370 375 380
	Gly 11e Gln Met Pro Ala Phe Ser Lys 11e Gly Gly 11e Leu Ala Asn	e Gly Gly Ile Leu Ala Asn	Tyr Gln Arg Arg Leu Ala Ala Val Ala Leu Ile Asn Ala Ala Ile Gln
	195 200	205	385 390 395 400
	Glu Leu Ser Val Asp Glu Ala Ala Leu His Ala Ala Val Ile Ala Ile	s Ala Ala Val Ile Ala Ile	Lys Gly Val Ala Glu Lys Thr Val Leu Glu Leu Met Asn Pro Glu Ala
	210 . 215 .		405 410 415
15	Asn Glu Ala Ile Asp Arg Arg Ile Pro Ala Asp Thr Phe Ala Ala Leu	a Asp Thr Phe Ala Ala Leu	15 Gln Leu Pro Gln Val Tyr Pro Phe Ala Ala Asp Leu Tyr Gln Lys Glu
	225 230	235 240	420 425 430
	Lys Asn Fro Asn Ala Met Leu Val Asn Leu Glu Glu Pro Leu Ala Ser	u Glu Glu Pro Leu Ala Ser	Leu Ala Thr Leu Gln Arg Gln Ser Pro Glu His Asn Leu Thr His Pro
	245 . 250	0 255	435 440 445
	Thr Tyr Gln Asp Ile Leu Tyr Gln Ala Lys Gln Asp Lys Met Thr Asn	s Gln Asp Lys Met Thr Asn	Glu Leu Ser Val Ala Val Glu Met Leu Ser Ser Val Ala Leu Ile Asn
70	260 265	270	20 450 455 460
	Ale Lys Asn Arg Thr Glu Asn Ser Glu Arg Glu Arg Asp Val Tyr Glu	g Glu Arg Asp Val Tyr Glu	Arg Ala Leu Glu Ser Gly Asp Val Asn Thr Val Trp Lys Gln Leu Ser
	275 280	285	465 470 . 475 480
	Glu Leu Leu Thr Gln Ala Glu Ile Gln Gly Asn Ile Asn Lys Val Asn	y Asn Ile Asn Lys Val Asn	Ser Ser Val Thr Gly Leu Thr Asn Ile Glu Glu Asn Cys Gln Arg
	290 295	300	-485 . 490 495

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Tyr Leu Asp Glu Leu Met Lys Leu Lys Ala Gln Ala His Ala Glu Asn	ys Leu Lys Ala Gln Ala R	its Ala Glu Asn	Trp Val Lys Gly Gly Tyr Tyr Tyr His Asn Leu Glu Thr Gln Glu	His Asn Leu Glu Thr Gln Glu
200	505	510	690 695	700
Asn Glu Phe Ile Thr Trp Asn Asp Ile Gln Ala Cys Val Asp His Val	sn Asp Ile Gin Ala Cys V	(al Asp His Val	Gly Gly Trp Asp Glu Pro Pro Asn Phe Val Gln Asn Ser Met Gln Leu	Val Gln Asn Ser Met Gln Leu
515	520, 5		705 710	715 720
5 Asn Leu Val Val Gln Glu Glu His Glu Arg Ile Leu Ala Ile Gly Leu	lu His Glu Arg Ile Leu A	ila ile Gly beu	Ser Arg Glu Glu 11e Gln Ser Ser 11e Ser Gly Vel Thr Ale Ala Tyr	Ser Gly Val Thr Ala Ala Tyr
530 53	535 . 540		725	730 735
' Ile Asn Glu Ala Leu Asp Glu Gly Asp Ala Gln Lys Thr Leu Gln Ala	lu Gly Asp Ala Gln Lys T	hr Leu Gln Ala	Asn Arg Glu Gln Leu Trp Leu Ala Asn Glu Gly Leu Ile Thr Arg Leu	3lu Gly Leu Ile Thr Arg Leu
545 550	555	. 095	740 745	750
Leu Gin ile Pro Ala Ala Lys Leu Glu Gly Val Leu Ala Glu Val Ala	/s Leu Glu Gly Val Leu A	la Glu Val Ala	Gin Ala Arg Cys Arg Gly Tyr Leu Val Arg Gin Glu Phe Arg Ser Arg	krg Gln Glu Phe Arg Ser Arg
10 565	570	575	755 760	765
Gln His Tyr Gln Asp Thr Leu Ile Arg Ala Lys Arg Glu Lys Ala Gln	u Ile Arg Ala Lys Arg G	lu Lys Ala Gln	Met Asn Phe Leu Lys Lys Gin Ile Pro Ala Ile Thr Cys Ile Gin Ser	la lle Thr Cys lle Gln Ser
280	585	. 069	770 775	. 780
Glu Ile Gln Asp Glu Ser Ala Val Leu Trp Leu As	a Val Leu Trp Leu Asp G	p Glu ile Gln Gly	Gln Trp Arg Gly Tyr Lys Gln Lys Lys Ale Tyr Gln Asp Arg Leu Ala	ila Tyr Gln Asp Arg Leu Ala
. 595	9		785 790	. 008
15 Gly Ile Trp Gln Ser Asn Lys Asp Thr Gln Glu Ala Gln Lys Phe Ala	s Asp Thr Gln Glu Ala Gl	in Lys Phe Ala	Tyr Leu Arg Ser His Lys Asp Glu Val Val Lys Ile Gln Ser Leu Ala	al Lys Ile Gln Ser Leu Ala
610 615	5 620		802·	810 815
Leu Gly Ile Phe Ala Ile Asn Glu Ala Val Glu Ser Gly Asp Val Gly	n Glu Ala Val Glu Ser Gl	LY Asp Val Gly	Arg Met His Gln Ala Arg Lys Arg Tyr Arg Asp Arg Leu Gln Tyr Phe	rg Asp Arg Leu Gln Tyr Phe
625 630	635	640	820 825	830
Lys Thr Leu Ser Ala Leu Arg Ser Pro Asp Val Gly Leu Tyr Gly Val	g Ser Pro Asp Val Gly Le	ou Tyr Gly Val	Arg Asp His Ile Asn Asp Ile Ile Lys Ile Gln Ala Phe Ile Arg Ala	le Gln Ala Phe Ile Arg Ala
20 645	650	. 655	835 840	845
lle Pro Glu Cys Gly Glu Thr Tyr His Ser Asp Leu Ala Glu Ala Lys	r Tyr His Ser Asp Leu Al	a Glu Ala Lys	Asn Lys Ala Arg Asp Tyr Lys Thr Leu Ile Asn Ala Glu Asp Pro	eu Ile Asn Ala Glu Asp Pro
	665	670	850 855	098
Lys Lys Lys Leu Ala Val Gly Asp Asn Asn Ser Lys Trp Val Lys His	y Asp Aen Aen Ser Lye Tr	p Val Lys His	Pro Met Val Val Ary Lys Phe Val His Leu Leu Asp Gln Ser Asp	is Leu Leu Asp Gln Ser Asp
675	680 · 685		865 870	875 880

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	WO 2004/05S519 89	PC 89/335	PCT/EP2003/014057	WO 2004/055519		90/335	PCT/EP2003/01
	Gln Asp Phe Gln Glu Glu Leu Asp Leu Met Lys Met Arg	Leu Mẹt Lys Met Arg Glu (Glu Glu Val	Arg Gln I	Arg Gln Ile Leu Ala Pro Val	Val Lys Glu ile Met	Авр Авр Сув
	885	068	895	1070	1075	1080	
	lle Thr Leu Ile Arg Ser Asn Gln Gln Leu Glu Asn Asp Leu Asn Leu	Gln Leu Glu Asn Asp Leu	Asn Leu	Ser Leu A	Ser Leu Asn Ile Lys Thr Asp Pro Val Asp Ile Tyr		Lys Ser Trp
	006	905 . 910		1085	1090	1095	
N.	Met Asp Ile Lys Ile Gly Leu Leu Val Lys Asn Lys Ile Thr Leu Gln	Val Lys Asn Lys Ile Thr	reu Gln		Val Asn Gln Met Glu Ser Gln Thr Gly Glu Ala Ser		Lys Leu Pro
	915 920	925		1100	1105	1110	
	Asp Val Val Ser His Ser Lys Lys Leu Thr Lys Lys Asn Lys Glu Gln	Leu Thr Lys Lys Asn Lys (Glu Gln	Tyr Asp V	Tyr Asp Val Thr Pro Glu Gln	Ala beu Ala His Glu	Glu Val Lys
	930 935	940		1115	1120	1125	•
	Leu Ser Asp Met Met Met Ile Asn Lys Gln Lys Gly Gly Leu Lys Ala	Lys Gln Lys Gly Gly Leu	Lys Ala	Thr Arg L	eu Asp Ser Ser Ile	Thr Arg Leu Asp Ser Ser Ile Arg Asn Met Arg Ala Val Thr Asp	Al Thr Asp
2	945	955.	960	1130	1135	1140	
	Leu Ser Lys Glu Lys Arg Glu Lys Leu Glu Ala Tyr Gin His Leu Phe	Leu Glu Ala Tyr Gln His	Leu Phe	Lys Phe L	Lys Phe Leu Ser Ala Ile Val	Ser Ser Val Asp Lys Ile Pro Tyr	lle Pro Tyr
	3965	076		1145	1150	. 1155	
	Tyr Leu Leu Gin Thr Asn Pro Thr Tyr Leu Ala Lys Leu Ile Phe Gin	Tyr beu Ala Lys Leu Ile	Phe Gln	Gly Met A	Gly Met Arg Phe Ile Ala Lys Val Leu Lys Asp Ser		Leu His Glu
	086	066 586		1160	1165	1170	
51	Met Pro Gln Asn Lys Ser Thr Lys Phe Met Asp	Ser Val	Ile Phe Thr 15		ro Asp Ala Gly Glu	Lys Phe Pro Asp Ala Gly Glu Asp Glu Leu Leu Lys	ile ile Gly
	995 1000	1005		1175	1180	1185	
	Leu Tyr Asn Tyr Ala Ser Asn Gln Arg Glu Glu	In Arg Glu Glu Tyr Leu Leu Leu	nen beu	Asn Leu L	eu Tyr Tyr Arg Tyr	Asn Leu Leu Tyr Tyr Arg Tyr Met Asn Pro Ala Ile	Val Ala Pro
	1010 . 1015	1020		1190	1195	1200	
	Arg Leu Phe Lys Thr Ala Leu Gln Glu Glu Ile	Lys	Ser Lys Val	Asp Ala P	Phe Asp Ile Ile Asp Leu Ser Ala Gly Gly		Gln Leu Thr
20	1025 1030	1035	. 20	1205	. 1210	1215	
	Asp Gln Ile Gln Glu Ile Val Thr Gly Asn Pro	Thr Val	Ile Lys	Thr Asp G	Gln Arg Arg Asn Leu	Gly Ser Ile Ala Lys . Met Leu Gln	Met Leu Gln
	1040 1045	1050		1220	1225	1230	
	Met Val Val Ser Phe Asn Arg Gly Ala Arg Gly	ly ala Arg Gly Gln Asn Ala Leu	la Leu	His Ala A	la Ser Asn Lys Met	His Ala Ala Ser Asn Lys Met Phe Leu Gly Asp Asn Ala His Leu	Ala His Leu
	1055	1065		1235	1240	1245	

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•																								
PCT/EP2003/014057	Ser Lys Ser		Lys Glu Lys		Thr Val Asp	•	Ala Arg Asp		Ala Glu Leu		Lys Ala Thr		Ile Lys Thr		Lys Lys Pro		Leu Lys Tyr		Glu Ile Glu		Glu Ile Ser		Lys Phe Met	
	Ile Arg Asp Ala Lys Thr Pro Asp Lys Met Lys Lys	1440	Glu Asp Ser Asn Leu Thr Leu Gln Glu Lys Lys Glu Lys	1455	ile Gin Thr Gly Leu Lys Lys Leu Thr Glu Leu Gly Thr Val Asp	1470	Pro Lys Asn Lys Tyr Gln Glu Leu Ile Asn Asp Ile Ala Arg Asp	1485	ile Arg Asn Gin Arg Arg Tyr Arg Gin Arg Arg Lys	1500		1515	Gly Glu Gln Val Asp Tyr Tyr Lys Ser Tyr	1530	Cys Leu Asp Asn Leu Ala Ser Lys Gly Lys Val Ser Lys Lys Pro	1545	Ser Lys Lys Ile Ser	1560	Thr Ala Ala Arg Leu His Glu Lys Gly Val Leu Leu Glu Ile Glu	1575	Lys Asn Val Ile Phe	1590	Pro Thr Glu Glu Val Gly Asp Phe Glu Val Lys Ala Lys Phe Met	1605
5519	Asp Ala Lys Thr Pro	0 1435		5 1450	Thr Gly Leu Lys Lys	0 1465	Asn Lys Tyr Gln Glu	. 1480	Asn Gln Arg Arg Tyr	1495	Val Lys Leu Gln Gln Thr Tyr Ala Ala Leu Aen Ser	1510		1525	Asp Asn Leu Ala Ser	1540	Arg Glu Met Lys Gly Lys Lys	1555	Ala Arg Leu His Glu	1570	Asp Leu Gln Val Asn Gln Phe Lys Asn Val Ile Phe	1585	Glu Glu Val Gly Asp	1600
WO 2004/055519	Ile Arg	1430	. Val Lys	1445	5 Ile Gln	. 1460	Pro Lys	1475	ile Arg	10. 1490	Val Lys	1505	Phe Tyr	1520	15 Cys Leu	1535	Arg Glu	1550	Thr Ale	. 20 1565	Asp Leu	1580	Pro Thr	1595
PCT/EP2003/014057	Lys Phe Arg		Gln Asp Lys		Thr Lys Pro		His Thr Leu		Asn Asp Pro		Thr Ile Glu		Pro Asn Lys		Thr Asn Lys		Ala Arg Thr		Ile Arg Phe		Pro Ala Thr		Arg Arg Ala	
91/335	Ser Gln Ser Tyr Gln Lys	1260	Asp Val Pro Glu Leu	1275	Asp Leu Val Thr Leu	1290	Glu Ile Ile Asn Thr	1305	Ile Ala Pro Glu His	1320.	Leu Gly Glu Val Pro	1335	Gly Asn Leu Asn Asp	1350	Val Ser Leu Thr Leu	1365	Asn Ala Glu Met Asp	1380	Leu Ile Val Asp Val	1395	Glu Ile Leu Glu Thr	1410	Gln Arg Ala Met Gln	. 1425
. 619	ile Asn Glu Tyr Leu	1255	Arg Phe Phe Gin Thr Ala Cys Asp Val Pro Giu Leu Gin	1270	Phe Asn Val Asp Glu Tyr Ser Asp Leu Val Thr Leu Thr	1285	Val ile Tyr ile Ser ile Gly Glu ile ile Asn Thr His	1300	Leu Leu 'Asp His Gln Asp Ala Ile Ala Pro Glu His Asn	1315	lle His Glu Leu Leu Asp Asp Leu Gly Glu Val Pro Thr	1330	Ser Leu Ile Gly Glu Ser Ser Gly Asn Leu Asn Asp Pro	1345	Glu Ala Leu Ala Lys Thr Glu Val Ser Leu Thr Leu	1360	Phe Asp Val Pro Gly Asp Glu Asm Ala Glu Met Asp Ala	1375	ile Leu Leu Asn Thr Lys Arg Leu Ile Val Asp Val	1390	Gin Pro Gly Glu Thr Leu Thr Glu Ile Leu Glu Thr Pro	1405	Ser Glu Gln Glu Ala Glu His Gln Arg Ala Met Gln Arg	1420
WO 2004/055519	Ser Ile	1250	Arg Phe	1265	5 Phe Asn (1280	Val Ile	1295	ren ren ,	10 1310	Ile His (1325	Ser Leu 1	1340	15 Glu Ala L	1355	Phe Asp V	1370	Ile Leu I	20 1385	Gln Pro 6	1400	Ser Glu G	1415

Ang Arg Lou Leu Lou Leu Lou Lys Lys Lys S Lys Lys S Lou Lou Lou Lou Lou Lou Lou	PCT/EP2003/014057 .	WO 2004/055519 PCT/EP2003/014057
hap Arg Lys Lys 5 Lys Lys 5 10 10 10 115 115	Gly Val Gln Met Glu Thr Phe Met Leu His Tyr Gln Asp Leu Leu	٠.
App Arg Lys Lys Lys Lys 10 10 11 115 115		Glu Leu Asn Asp Leu Phe Lys Ala Ala Cys Leu Pro Leu Pro Gly Tyr
bys Lys 10 10 115 115 115	Phe	. 07
Lys Lys 10 10 11 15 15 15 15		Arg Val Arg Glu Ile Thr Glu Asn Leu Met Ala Thr Gly Asp Leu Asp
10 15 15 15 15 15 15 15 15 15 15 15 15 15		. 50
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10 16 15 15 15 15 15 15 15 15 15 15 15 15 15		. 01
10 15 15 Arg Glu 15		Leu Lys Ser Thr Asp Val Ala Lys Thr Phe Arg Lys Ala Ile Asn Lys
15 15 20 20 15 15 15 15 15 15 15 15 15 15 15 15 15		-
15 15 20 20 15 15 15 15 15 15 15 15 15 15 15 15 15		10 Lys Glu Gly Ile Cys Ala Ile Gly Gly Thr Ser Glu Gln Ser Ser Val
15 15 20 20 15 15 15 15 15 15 15 15 15 15 15 15 15		
15. 20. 20. 15. 15. 15. 15. 15. 15. 15. 15. 15. 15		Gly Thr Gln His Ser Tyr Ser Glu Glu Glu Lys Tyr Ala Phe Val Asn
15. 20. 20. 15. 15. 15. 15. 15. 15. 15. 15. 15. 15		120
15. 15. 20. 20. 15. 15. 15. 15. 15. 15. 15. 15. 15. 15		Trp Ile Asn Lys Ala Leu Glu Asn Asp Pro Asp Cys Arg His Val Ile
20 Arg Glu 15		130 135
20 Arg Glu 15	L-plastin (Lymphocyte cytosolic protein 1)	. Pro Met Asn Pro Asn Thr Asn Asp Leu Phe Asn Ala Val Gly Asp Gly
20 Arg Glu 15		150
20 Arg Glu 15	ав оf 09 Dec 2002; Р13796	Ile Val Leu Cys Lys Met Ile Asn Leu Ser Val Pro Asp Thr Ile Asp
20 Arg Glu		
Arg Glu 15		20 Glu Arg Thr Ile Asn Lys Lys Leu Thr Pro Phe Thr Ile Gln Glu
Arg Glu 15		
15 200		Asn Leu Asn Leu Ala Leu Asn Ser Ala Ser Ala Ile Gly Cys His Val
		. 200
Ala Phe Ala Lys Val Asp Thr Asp Gly Asn Gly Tyr Ile Ser Phe Asn		Val Asn Ile Gly Ala Glu Asp Leu Lys Glu Gly Lvs Pro Tvr Len Val

210 210 211 212 212 213 214 215 216 217 218 219 219 219 219 219 219 219	### PCT/PEP10030014053519 405 410 415 777 Ser Amp Leu Ser Amp Ala Leu Val Ile Phe Gin Leu Tyr Giu Lya 420 420 430 11e Lya Val Pro Val Amp Trp Amn Ary Val Amn Lya Pro Pro Tyr Pro 5 435 Lya Leu Gly Gly Amn Met Lya Lya Leu Glu Amn Cya Amn Tyr Ala Val 450 450 Glu Leu Gly Lya Amn Gin Ala Lya Phe Ser Leu Val Gly Ile Gly Gly 465 470 485 485 480 Gln Leu Met Ary Ary Tyr Thr Leu Amn Ile Leu Glu Glu Ile Gly Gly 500 Gly Gln Lya Val Amn Amp Thr Leu Amn Ile Leu Glu Glu Ile Gly Gly 500 510 Gly Gln Lya Val Amn Amp Amp Ile Ile Val Amn Trp Val Amn Glu Thr 15 515 520 520 530 540 199 Ile Ser Thr Ser Leu Pro Val Leu Amp Leu Lau Lya Dan Ile Gln 540 540 550 540 550 540 550 540 550 550 540 550 550 550 550 550 560 570 57
370 375 380	
Ile Asp Trp Gly Ala Leu Glu Gly Glu Thr Arg Glu Glu Arg Thr Phe 385 390 400	Asn Ala Lys Tyr Ala Ile Ser Met Ala 585
Arg Asm Tro Met Asm Ser Leu Glv Val Asm Pro Arg Val asm His Leu	tral mere also are also dis-

WO 2004/055519	97/335	PCT/EP2003/014057	WO 2004/055519		PCT/EP2003/014057
595	600 605		50	25 60	
Pro Lys Met Val Met Thr Val Phe Ala Cys Leu Met Gly		Lys Gly Met	Asp Thr Ala Gly Gln G	Asp Thr Ala Gly Gln Glu Lys Phe Gly Gly Leu Arg Asp Gly Tyr Tyr	ፀ ነሃ ኪ ሃፑ ኪሃፑ
610 615	620		65	70 75	08
Lys Arg Val			ile Gln Ala Gln Cys A	Ile Gin Ala Gin Cys Ala Ile Ile Met Phe Asp Val Thr Ser Arg Val	Ser Arg Val
625	٠			06	95
			Thr Tyr Lys Asn Val	Thr Tyr Lys Asn Val Pro Asn Trp His Arg Asp Leu Val Arg Val Cys	Arg Val Cys
			100	105	110
<210> 27			Glu Asn Ile Pro Ile V	Glu Asn Ile Pro Ile Val Leu Cys Gly Asn Lys Val Asp Ile Lys Asp	Ile Lys Asp
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<213> Homo sapiens			130	135 140	
<220>			Gln Tyr Tyr Asp Ile S	Gln Tyr Tyr Asp Ile Ser Ala Lys Ser Asn Tyr Asn Phe Glu Lys Pro	Glu Lys Pro
<221> GTP-binding nuclear protein RAN	otein RAN		145	150 . 155	160
<222> (1)(216)		•	Phe Leu Trp Leu Ala A	Phe Leu Trp Leu Ala Arg Lys Leu Ile Gly Asp Pro Asn Leu Glu Phe	Leu Glu Phe
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<400> 27	•		Val Ala Met Pro Ala I	Val Ala Met Pro Ala Leu Ala Pro Pro Glu Val Val Met Amp Pro Ala	Asp Pro Ala
			180	185	190
Met Ala Ala Gln Gly Glu Pro Gln Val Gln Phe Lys Leu Val Leu Val	in Val Gin Phe Lys Leu V	al Leu Val	Leu Ala Ala Gln Tyr G	Leu Ala Ala Gln Tyr Glu His Asp Leu Glu Val Ala Gln Thr Thr Ala	Thr Thr Ale
1 5	10		. 195	200 205	
Gly Asp Gly Gly Thr Gly Lys Thr Thr Phe Val Lys Arg His Leu Thr	hr Thr Phe Val Lys Arg H.		20 Leu Pro Asp Glu Asp Asp Asp Leu	sp Asp Leu	
20	25 30		210	215	
Gly Glu Phe Glu Lys Lys Tyr Val Ala Thr Leu Gly Val Glu Val His	al Ala Thr Leu Gly Val G	lu Val His			
35 40	0 45				٠.
Pro Leu Val Phe His Thr Asn Axg Gly Pro Ile Lys Phe Asn Val Trp	rg Gly Pro Ile Lys Phe As	sn Val Trp	<210> 28		

WO 2004/055519 PCT/EP2003/014057 99/335	WO 2004/055519 PCT/EP1003/014057
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<213> Homo sapiens	130 135 140
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5 <221> Heterogeneous nuclear ribonucleoprotein K	5 145 150 155 160
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1 5 10 15	205 200 205
Gly Glu Phe Gly Lys Arg Pro Ala Glu Asp Met Glu Glu Glu Gln Ala	ile Leu Asp Leu ile Ser Glu Ser Pro Ile Lys Gly Arg Ala Gln Pro
20 25 30	210 215 220
Phe Lys Arg Ser Arg Asn Thr Asp Glu Met Val Glu Leu Arg Ile Leu	Tyr Asp Pro Asn Phe Tyr Asp Glu Thr Tyr Asp Tyr Gly Gly Phe Thr
15 35 40 45	15 225 230 235 240
Leu Gln Ser Lys Asn Ala Gly Ala Val Ile Gly Lys Gly Gly Lys Asn	Met Met Phe Asp Asp Arg Arg Gly Arg Pro Val Gly Phe Pro Met Arg
50 55 60	245 250 255
ile Lys Ala Leu Arg Thr Asp Tyr Asn Ala Ser Val Ser Val Pro Asp	Gly Arg Gly Gly Phe Asp Arg Met Pro Pro Gly Arg Gly Gly Arg Pro
65 70 75 80	260 265 270
20 Ser Ser Gly Pro Glu Arg Ile Leu Ser Ile Ser Ala Asp Ile Glu Thr	20 Met Pro Pro Ser Arg Arg Asp Tyr Asp Asp Met Ser Pro Arg Arg Gly
	275 280 285
Ile Gly Glu Ile Leu Lys Lys Ile Ile Pro Thr Leu Glu Glu Gly Leu	Pro Pro Pro Pro Pro Gly Arg Gly Gly Arg Gly Gly Ser Arg Ala
100 105 110	290 295 300
Gln Leu Pro Ser Pro Thr Ala Thr Ser Gln Leu Pro Leu Glu Ser Asp	Arg Asn Leu Pro Leu Pro Pro Pro Pro Pro Arg Gly Gly Asp Leu

WO 2004/055519 PCT/EP2003/014057 101/335	WO 2004/055519 PCT/EP2003/014057
305 310 315 320	<213> Homo sapiens
Met Ala Tyr Asp Arg Arg Gly Arg Pro Gly Asp Arg Tyr Asp Gly Wet	<22.0>
325 330 335	<221> Translationally controlled tumor protein (TCTP)
Val Gly Phe Ser Ala Asp Glu Thr Trp Asp Ser Ala Ile Asp Thr Trp	<222> (1)(172)
340 345 350	5 <223> Accession No. as of 09 Dec 2002: P13693
Ser Pro Ser Glu Trp Gln Met Ala Tyr Glu Pro Gln Gly Gly Ser Gly	<400> 29
355 360 365	
Tyr Asp Tyr Ser Tyr Ala Gly Gly Arg Gly Ser Tyr Gly Asp Leu Gly	Met ile ile Tyr Arg Asp Leu ile Ser His Asp Glu Met Phe Ser Asp
370 375 380	1 5 10 15
Gly Pro lle lle Thr Thr Gln Val Thr 11e Pro Lys Asp Leu Ala Gly	10 Ile fyr Lys Ile Arg Glu Ile Ala Asp Gly Leu Cys Leu Glu Val Glu
385 390 395 400	20 25 30
Ser Ile Ile Gly Lys Gly Gly Gln Arg Ile Lys Gln Ile Arg His Glu	Gly Lys Met Val Ser Arg Thr Glu Gly Asn Ile Asp Asp Ser Leu Ile
405 410 415	35 40 45
Ser Gly Ala Ser Ile Lys Ile Asp Glu Pro Leu Glu Gly Ser Glu Asp	Gly Gly Asn Ala Ser Ala Glu Gly Pro Glu Gly Glu Gly Thr Glu Ser
420 425 430	15 50 55 60
Arg ile ile Thr ile Thr Gly Thr Gln Asp Gln ile Gln Asn Ala Gln	Thr Val Ile Thr Gly Val Asp Ile Val Met Asn His His Leu Gln Glu
435 440 445	65 . 70 75 . 80
Tyr Leu Leu Gln Asn Ser Val Lys Gln Tyr Ser Gly Lys Phe Phe	Thr Ser Phe Thr Lys Glu Ala Tyr Lys Lys Tyr Ile Lys Asp Tyr Met
450 455 . 460	56 .06 58 .
	20 Lys Ser Ile Lys Gly Lys Leu Glu Glu Gln Arg Pro Glu Arg Val Lys
	100 105 110
<210> 29	Pro Phe Met Thr Gly Ala Ala Glu Gln Ile Lys His Ile Leu Ala Asn
<211 > 172	. 115 120 125
<212> PRT	Phe Lys Asn Tyr Gln Phe Phe Ile Gly Glu Asn Met Asn Pro Asp Gly

WO 2004/055519 PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057 104/335
130 135 · 140	
Met Val Ala Leu Leu Asp Tyr Arg Glu Asp Gly Val Thr Pro Tyr Met	Lys Asp Ala Gln Glu Lys Leu Glu Leu Ala Glu Lys Lys Ala Thr Asp
145 150 155 160	65 . 70 75 80
Ile Phe Phe Lys Asp Gly Leu Glu Met Glu Lys Cys	Ala Glu Ala Asp Val Ala Ser Leu Asn Arg Arg Ile Gln Leu Val Glu
5 165 170	56 06 58 5
	Glu Glu Leu Asp Arg Ala Gln Glu Arg Leu Ala Thr Ala Leu Gln Lys
	100 105 110
<210> 30	Leu Glu Glu Ala Glu Lys Ala Asp Glu Ser Glu Arg Gly Met Lys
<211> 284	115 120 125
0 <212> PRT	10 Val Ile Glu Ser Arg Ala Gln Lys Asp Glu Glu Lys Met Glu Ile Gln
<213> Homo sapiens	130 135 140
. <220>	Glu ile Gin beu Lys Glu Ala Lys His ile Ala Glu Asp Ala Asp Arg
<221> Tropomyosin 1 alpha chain	145 150 155 160
<222> (1)(284)	Lys Tyr Glu Glu Val Ala Arg Lys Leu Val Ile Ile Glu Ser Asp Leu
5 <223> Accession No. as of 06 Dec 2002; P09493	15 165 170 175
<400> 30	Glu Arg Ala Glu Glu Arg Ala Glu Leu Ser Glu Gly Lys Cys Ala Glu
	180 185 190
Met Asp Ala ile Lys Lys Lys Met Gln Met Leu Lys Leu Asp Lys Glu	Leu Glu Glu Glu Leu Lys Thr Val Thr Asn Asn Leu Lys Ser Leu Glu
1 5 10 15	195 200 205
) Asn Ala Leu Asp Arg Ala Glu Gln Ala Glu Ala Asp Lys Lys Ala Ala	20 Ala Gln Ala Glu Lys Tyr Ser Gln Lys Glu Asp Arg Tyr Glu Glu
20 25 30	210 . 215 220
Glu hap Arg Ser Lys Gln Leu Glu Asp Glu Leu Val Ser Leu Gln Lys	ile Lys Val Leu Ser Asp Lys Leu Lys Glu Ala Glu Thr Arg Ala Glu
35 .40 45	225 230 235 240
Lys Leu Lys Gly Thr Glu Asp Glu Leu Asp Lys Tyr Ser Glu Ala Leu	Phe Ala Glu Arg Ser Val Thr Lys Leu Glu Lys Ser Ile Asp Asp Leu

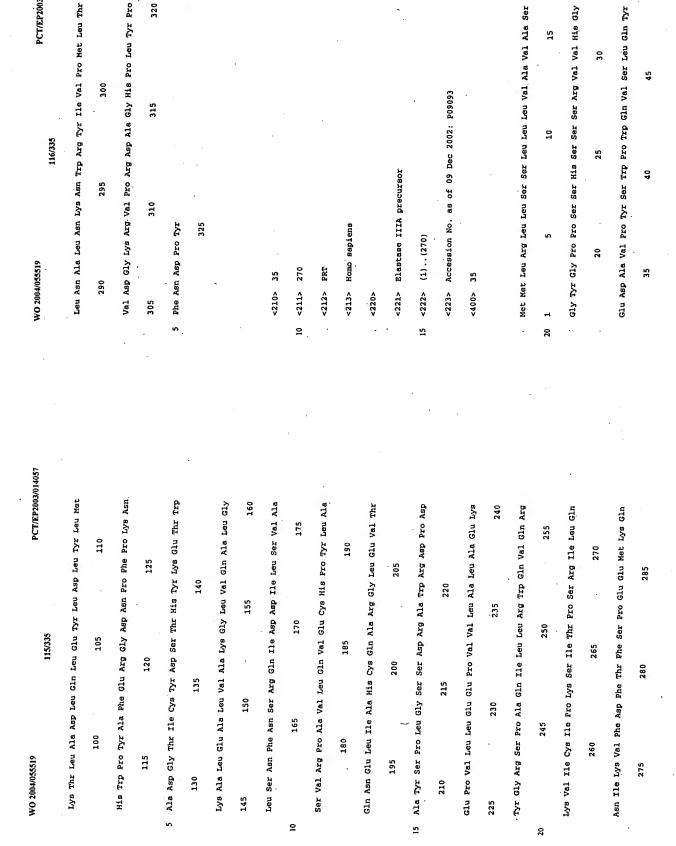
WO 2004/055519	10677361	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/014057
	105/555		106/335	
. 245	. 250	255	90 22.	9.0
Glu Asp Glu Leu Tyı	Glu Asp Glu Leu Tyr Ala Gln Lys Leu Lys Tyr Lys Ala	. Ile Ser Glu	Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu	et Ala Ile Arg Leu
260	265	270	65 70 75	80
Glu beu Asp His Ale	Glu Leu Asp His Ala Leu Asn Asp Met Thr Ser Ile		Arg Gly Met Asp Leu Glu Glu Thr Ser Val Leu Thr Gln Ale Leu Ale	hr Gln Ale Leu Ale
5 275	. 280		. 06	95
			Gin Ser Gly Gin Gin Leu Giu Trp Pro Giu Ala Trp Arg Gin Gin Leu	rp Arg Gln Gln Leu
			100	110
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<211> 482			115 120	125
10 <212> PRT			10 Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met 11e Ser	al Pro Met Ile Ser
<213> Homo sapiens			130 135 1	. 140
<220>			Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser	op Lys Leu Glu Ser
<221> Thymidine ph	Thymidine phosphorylase precursor		145 150 155	160
<222> (1)(482)			lle Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu	in Met Gin Val Leu
15 <223> Accession No	Accession No. as of 09 Dec 2002: P19971		15 . 165 170	175
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			180 185	190
Met Ala Ala Leu Met	Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro	Ala Pro Gly	Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Vel Thr Ala Thr Val	il Thr Ala Thr Val
1	10		195 200	205
20 Asp Phe Ser Gly Glu	Asp Phe Ser Gly Glu Gly Ser Gln Gly Leu Pro Asp Pro	Ser Pro Glu	20 Asp Ser Leu Pro Leu lle Thr Ala Ser Ile Leu Ser Lys Lys Leu Val	r Lys Lys Leu Val
20	25	30	210 215 . 22	220
Pro Lys Gln Leu Pro	Pro Lys Gln Leu Pro Glu Leu Ile Arg Met Lys Arg Asp	Gly Gly Arg	Glu Gly Leu Ser Ala Leu Val Val Asp Val Lys Phe Gly Gly Ala Ala	ie Gly Gly Ala Ala
35	. 40 45		225 230 235	. 240
Leu Ser Glu Ala Asp	Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val	Val Asn Gly	Val Phe Pro Asn Gln Glu Gln Ala Arg Glu Leu Ala Lys Thr Leu Val	a Lys Thr Leu Val

	WO 2004/055519	QF	107/336	PCT/EP2003/014057	WO 2004/055519		PCT/EP2003/014057
			2001			108/335	
		245	250	. 255	435	440	445
	Gly Val Gly Al	la Ser Leu Gly Leu	Gly Val Gly Ala Ser Leu Gly Leu Arg Val Ala Ala Ala Leu Thr Ala	Leu Thr Ala	Gly Pro Gln Ser Arg Ala	Gly Pro Gln Ser Arg Ala Leu Gln Glu Ala Leu Val Leu Ser Asp Arg	. Leu Ser Asp Arg
	260		265		450	455 460	
	Met Asp Lys Pr	o Leu Gly Arg Cys	Met Asp Lys Pro Leu Gly Arg Cys Val Gly His Ala Leu Glu Val Glu	Glu Val Glu	Ala Pro Phe Ala Ala Pro	Ala Pro Phe Ala Ala Pro Leu Pro Phe Ala Glu Leu Val Leu Fro Pro	. Val Leu Pro Pro
	5 275	. 280	285		5 465 . 470	. 475	480
	Glu Ala Leu Le	u Cys Met Asp Gly	Glu Ala Leu Leu Cys Met Asp Gly Ala Gly Pro Pro Asp Leu Arg Asp	Leu Arg Asp	Gln Gln		
	290	295	300				
	Leu Val Thr Th	r Leu Gly Gly Ala	Leu Val Thr Thr Leu Gly Gly Ala Leu Leu Trp Leu Ser Gly His Ala	бју нів Ада			
	305	310	315	320			
9		a Gln Gly Ala Ala	Gly Thr Gln Ala Gln Gly Ala Ala Arg Val Ala Ala Ala Leu Asp Asp		10 <210> 32		
		325	330	335	<211> 488		
	Gly Ser Ala Let	u Gly Arg Phe Glu /	Gly Ser Ale Leu Gly Arg Phe Glu Arg Met Leu Ala Ala Gln Gly Val	Gln Gly Val	<212> PŘT	<i>x</i> .	
	340		345	350	<213> Homo sapiens		
	Asp Pro Gly Leu	u Ala Arg Ala Leu (Asp Pro Gly Leu Ala Arg Ala Leu Cys Ser Gly Ser Pro Ala Glu Arg	Ala Glu Arg	<220>		
15		360	365	sı	i <221> Cytosol aminopeptidase	:1dase	-
	Arg Gln Leu Leu	1 Pro Arg Ala Arg C	Arg Gln Leu Leu Pro Arg Ala Arg Glu Glu Glu Leu Leu Ala Pro	Leu Ala Pro	<222> (1) (488)		
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	Ala Asp Gly Thr	r Val Glu Leu Val A	Ala Asp Gly Thr Val Glu Lou Val Arg Ala Leu Pro Leu Ala Leu Val	Ala Leu Val	<400> 32		
	385	390	395	400		•	·
20		Gly Ala Gly Arg S	Leu His Glu Leu Gly Ala Gly Arg Ser Arg Ala Gly Glu Pro Leu Arg	Pro Leu Arg . 20	Wet Thr Lys Gly Leu Val Leu Gly Ile Tyr Ser Lys Glu Lys Glu Asp	Leu Gly Ile Tyr Ser Lys	Glu Lys Glu Asp
		405	410	415	, td	10	1.5
	Leu Gly Val Gly	'Ala Glu Leu Leu V	Leu Gly Val Gly Ala Glu Leu Leu Val Asp Val Gly Gln Arg Leu Arg	Arg Leu Arg	Asp Val Pro Gin Phe Thr Ser Ala Gly Glu Asn Phe Asp Lys Leu Leu	Ser Ala Gly Glu Asn Phe	Авр Гув Leu Leu
	420		425	430	50	25	30
	Arg Gly Thr Pro	Trp Leu Arg Val H	Arg Gly Thr Pro Trp Leu Arg Val His Arg Asp Gly Pro Ala Leu Ser	Ala Leu Ser	Ala Gly Lys Leu Arg Glu Thr Leu Asn 11e Ser Gly Pro Pro Leu Lys	Thr Leu Asn Ile Ser Gly	Pro Pro Leu Lys

CT/EP2003/014057 WO 2004/055519	. 225	Ala Asn Glu Pro Pro Leu Val Phe Val Gly Lys Gly Ile Thr Phe Asp	245	Ser Gly Gly Ile Ser Ile Lys Ala Ser Ala Asn Met Asp Leu Met Arg	5 260 265	Ala Asp Met Gly Gly Ala Ala Thr Ile Cys Ser Ala Ile Val Ser Ala	275 280	Ala Lys Leu Asn Leu Pro Ile Asn Ile Ile Gly Leu Ala Pro Leu Cys	290 295 .	u Glu Asn Met Pro Ser Gly Lys Ala Asn Lys Pro Gly Asp Val Val Arg	305 310	Ala Lys Asn Gly Lys Thr. Ile Gln Val Asp Asn Thr Asp Ala Glu Gly	. 325	arg Leu Ile Leu Ala Asp Ala Leu Cys Tyr Ala His Thr Phe Asn Pro	346 346 348	1 Lys Val Ile Leu Asn Ala Ala Thr Leu Thr Gly Ala Met Asp Val Ala	355	Leu Gly Ser Gly Ala Thr Gly Val Phe Thr Asn Ser Ser Trp Leu Trp	370 375	20 Asn Lys Leu Phe Glu Ala Ser Ile Glu Thr Gly Asp Arg Val Trp Arg	385 390	Met Pro Leu Phe Glu His Tyr Thr Arg Gln Val Val Asp Cys Gln Leu
WO 2004/055519 PCT/EP2000	35 40 45	Ala Gly Lys Thr Arg Thr Phe Tyr Gly Leu His Gln Asp Phe Pro Ser	09 55 05	Val Val Leu Val Gly Leu Gly Lys Lys Ala Ala Gly Ile Asp Glu Gln	65 70 75 80	Glu Asn Trp His Glu Gly Lys Glu Asn Ile Arg Ala Ala Val Ala Ala	95 90	Gly Cys Arg Gln Ile Gln Asp Leu Glu Leu Ser Ser Val Glu Val Asp	. 100 105 110	Pro Cys Gly Asp Ala Gln Ala Ala Ala Glu Gly Ala Val Leu Gly Leu	115 120 125	Tyr Glu Tyr Asp Asp Leu Lys Gln Lys Lys Lys Met Ala Val Ser Ala	130	Lys Leu Tyr Gly Ser Gly Asp Gln Glu Ala Trp Gln Lys Gly Val Leu	145 . 150 . 155 . 160	Phe Ala Ser Gly Gln Asn Leu Ala Arg Gln Leu Met Glu Thr Pro Ala	165 · 170 175	Asn Glu Met Thr Pro Thr Arg Phe Ala Glu Ile Ile Glu Lys Asn Leu	160 . 185 190	Lys Ser Ala Ser Ser Lys Thr Glu Val His Ile Arg Pro Lys Ser Trp	200 205	Ile Glu Glu Gln Ala Met Gly Ser Phe Leu Ser Val Ala Lys Gly Ser

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	111/335				112/335	
420	425	430		•	Gly Leu Gly Gly Gly Ser Val Arg Phe Gly Pro Gly Val Ala Phe Arg	Br
Ala Ala Ala Phe Leu Lys Glu Phe Val Thr His Pro Lys	e Val Thr His Pro Ly	's Trp Ala His			20 25 30	. *
435 440	10 445				Ala Pro Ser Ile His Gly Gly Ser Gly Gly Arg Gly Val Ser Val Ser	
Leu Asp Ile Ala Gly Val Met Thr Asn Lys Asp Glu Val	ır Asn Lys Asp Glu Va	d Pro Tyr Leu			35 . 40 45	
450 455	460			50	Ser Ala Arg Phe Val Ser Ser Ser Ser Gly Gly Gly Gly Gly	ly.
Arg Lys Gly Met Thr Gly Arg Pro Thr Arg Thr Leu Ile Glu Phe Leu	o Thr Arg Thr Leu Il	e Glu Phe Leu			90 55 05	
465	475	480			Tyr Gly Gly Val Leu Thr Ala Ser Asp Gly Leu Leu Ala Gly Asn Glu	PI
Leu Arg Phe Ser Gln Asp Asn Ala	ď				65 70 75 80	
485			,	:	Lys Leu Thr Met Gin Asn Leu Asn Asp Arg Leu Ala Ser Tyr Leu Asp	<u>Q</u>
				01	56 06 . 58	
				٠	Lys Val Arg Ala Leu Glu Ala Ala Asn Gly Glu Leu Glu Val Lys Ile	ej
<210> 33					001	
<211> 400					Arg Asp Try Tyr Gln Lys Gln Gly Pro Gly Pro Ser Arg Asp Tyr Ser	ı
<212> PRT					115 120 125	
<213> Homo sapiens				15	His Tyr Tyr Thr Thr Ile Gln Asp Leu Arg Asp Lys Ile Leu Gly Ale	ej.
<220>	-				130 135 140	
<221> Keratin, type I cytoskeletal 19	letal 19			-	Thr Ile Glu Asn Ser Arg Ile Val Leu Gln Ile Asp Asn Ala Arg Leu	n
<222> (1)(400)	•				145 150 155 160	. 0
<223> Accession No. as of 09 Dec 2002 ; P08727	Dec 2002 : P08727				Ala Ala Asp Asp Phe Arg Thr Lys Phe Glu Thr Glu Gln Ala Leu Arg	5 0
				8	165 , 170 , 175	
<400> 33					Met Ser Val Glu Ala Asp Ile Asn Gly Leu Arg Arg Val Leu Asp Glu	2
					180 185 190	
Met Thr Ser Tyr Ser Tyr Arg Gln Ser Ser Ala Thr. Ser	ı Ser Ser Ala Thr. Ser	Ser Phe Gly			Leu Thr Leu Ala Arg Thr Asp Leu Glu Met Gln Ile Glu Gly Leu Lys	
. 55	10	15		•	195 200 205	

	WO 2004/055519	113/335	PCT/EP2003/014057		WO 2004/055519 114/335	PCT/EP2003/0
	Glu Glu Leu Ala Tyr Leu Lys Lys Asn His Glu	ys Lys Asn His Gl	lu Glu Glu Ile Ser Thr	H		
	210 2	215	220			
	Leu Arg Gly Gln Val Gly Gly Gln Val Ser Val	ly Gln val Ser Va	al Glu Val Asp Ser Ala	g;	<210> 34	
	225 230	23	235 240	. 01	<211> 325	
'n	Pro Gly Thr Asp Leu Ala Lys Ile Leu Ser Asp	ys Ile Leu Ser As	Bp Met Arg Ser Gln Tyr	£.	<212> PRT	
	245	250	255		<213> Homo sapiens	
	Glu Val Met Ala Glu Gln Asn Arg Lys Asp Ala	sn Arg Lys Asp Al	la Glu Ala Trp Phe Thr	H	<220>	
	260	265	270		<221> Alcohol dehydrogenase [NADP+]	
	Ser Arg Thr Glu Glu Leu Asn Arg Glu Val Ala	sn Arg Glu Val Al	la Gly His Thr Glu Gln	rļ.	<222> (1)(325)	
10	275	280	285	. 10	<223> Accession No. as of 09 Dec 2002: P14550	14550
	Leu Gln Met Ser Arg Ser Glu Val Thr Asp Leu Arg Arg Thr Leu Gln	lu Val Thr Asp Le	eu Arg Arg Thr Leu Gli	Ħ.	<400> 34	
	290 2	295	300			
	Gly Leu Glu Ile Glu Leu Gln Ser Gln Leu Ser	ln Ser Gln Leu Se	er Met Lys Ala Ala Leu	n.	Met Ala Ala Ser Cys Val Leu Leu His Thr Gly Gln Lys Met Pro Leu	ly Gln Lys Met Pro Leu
	305 . 310	315	320		. 10	15
15	Glu Asp Thr Leu Ala Glu Thr Glu Ala Arg.Phe Gly Ala Gln Leu Ala	hr Glu Ala Arg Ph	10 Gly Ala Gln Leu Ale	. 81	Ile Gly Leu Gly Thr Trp Lys Ser Glu Pro Gly Gln Val Lys Ala Ala	ly Gln Val Lys Ala Ala
•	325	330	335		20 25	30
	His Ile Gln Ala Leu Ile Ser Gly Ile Glu Ala Gln Leu Ala Asp Val	er Gly Ile Glu Al	la Gln Leu Ala Asp Val	Ti.	Val Lys Tyr Ala Leu Ser Val Gly Tyr Arg His Ile Asp Cys Ala Ala	is ile Asp Cys Ala Ala
	340	345	350		35 40	45
	Arg Ala Asp Ser Glu Arg Gln Asn Gln Glu Tyr Gln Arg Leu Met Asp	ln Asn Gln Glu Ty	r Gln Arg Leu Met Asp		Ile Tyr Gly Asn Glu Pro Glu Ile Gly Glu Ala Leu Lys Glu Asp Val	la Leu Lys Glu Asp Val
20	355	360	365	20	50 55	09
	Ile Lys Ser Arg Leu Glu Glu Glu Ile Ala Thr Tyr Arg Sex Leu Leu	ln Glu Ile Ala Th	ır Tyr Arg Ser beu bet		Gly Pro Gly Lys Ala Val Pro Arg Glu Glu Leu Phe Val Thr Ser Lys	eu Phe Val Thr Ser Lys
	370 37	375	380		65 70 70	75 80
	Glu Gly Gln Glu Asp His Tyr Asn Asn Leu Ser Ala Ser Lys .Val Leu	yr Asn Asn Leu Se	n Ala Ser Lys Val Leu		Leu Trp Asn Thr Lys His His Pro Glu Asp Val Glu Pro Ala Leu Arg	al Glu Pro Ala Leu Arg
	385 . 390	395	95 400	•	85	95



WO 2004/055519 PCT/EP2003/014057	57 WO 2004/055519 PCT/EP2003/014057
117/335	118/335
Glu Lys Ser Gly Ser Phe Tyr His Thr Cys Gly Gly Ser Leu Ile Ala	Gly Phe Gly Cys Asn Phe 11e Trp Lys Pro Thr Val Phe Thr Arg Val
50 55 60	245 250 255
Pro Asp Trp Vel Val Thr Ala Gly His Cys Ile Ser Arg Asp Leu Thr	Ser Ala Phe Ile Asp Trp Ile Glu Glu Thr Ile Ala Ser His
65 70 75 80°	260 265 270
i Tyr Gln Val Val Leu Gly Glu Tyr Asn Leu Ala Val Lys Glu Gly Pro	S. C.
95 . 90 . 95	
Glu Gln Val Ile Pro Ile Asn Ser Glu Glu Leu Phe Val His Pro Leu	<210> 36
100 105 110	<211> 509
Trp Asn Arg Ser Cys Val Ala Cys Gly Asn Asp Ile Ala Leu Ile Lys	<212> PRT .
115 120 125	10 <213> Ното варіелв
Leu Ser Arg Ser Ala Gln Leu Gly Asp Ala Val Gln Leu Ala Ser Leu	<220>
130 135 140	<221> Dihydrolipoamide dehydrogenase, mitochondrial precursor
Pro Pro Ala Gly Asp Ile Leu Pro Asn Lys Thr Pro Cys Tyr Ile Thr	<222> (1)(509)
145 . 150 155 160	<223> Accession No. as of 09 Dec 2002: P09622
Gly Trp Gly Arg Leu Tyr Thr Asn Gly Pro Leu Pro Asp Lys Leu Gln	
165 170 175	
Gin Ala Arg Leu Pro Val Val Asp Tyr Lys His Cys Ser Arg Trp Asn	Met Gln Ser Trp Ser Arg Val Tyr Cys Ser Leu Ala Lys Arg Gly His
180 . 185 190	
Trp Trp Gly Ser Thr Val Lys Lys Thr Met Val Cys Ala Gly Gly Tyr	Phe Asn Arg Ile Ser His Gly Leu Gln Gly Leu Ser Ala Val Pro Leu
200 . 205	20 20 25 30
lle Arg Ser Gly Cys Asn Gly Asp Ser Gly Gly Pro Leu Asn Cys Pro	Arg Thr Tyr Ala Asp Gln Pro Ile Asp Ala Asp Val Thr Val Ile Gly
210 215 220	35 40 . 45
Thr Glu Asp Gly Gly Trp Gln Val His Gly Val Thr Ser Phe Val Ser	Ser Gly Pro Gly Gly Tyr Val Ala Ala Ile Lys Ala Ala Gln Leu Gly
225 230 235 240	. 60 . 55

WO 2004/055519 PCT/EP2003/014057 '	
Phe Lys Thr Val Cys Ile Glu Lys Asn Glu Thr Leu Gly Gly Thr Cys	
65 70 75 80	
Leu Aen Val Gly Cys Ile Pro Ser Lys Ala Leu Leu Asn Asn Ser His	
85 90 95	
Tyr Tyr His Met Ala His Gly Thr Asp Phe Ala Ser Arg Gly Ile Glu	
100 105 110	
Met Ser Glu Val Arg Leu Asn Leu Asp Lys Met Met Glu Gln Lys Ser	
115 120 . 125	
Thr Ala Val Lys Ala Leu Thr Gly Gly Ile Ala His Leu Phe Lys Gln	
130 135 140	
Asn Lys Val Val His Val Asn Gly Tyr Gly Lys 11e Thr Gly Lys Asn	
145 150 . 155 160	•
Gln Val Thr Ala Thr Lys Ala Asp Gly Gly Thr Gln Val Ile Asp Thr	
165 170 175	
Lys Asn Ile Leu Ile Ala Thr Gly Ser Glu Val Thr Pro Phe Pro Gly	
180 185 190	
ile Thr ile Asp Glu Asp Thr ile Val Ser Ser Thr Gly Ala Leu Ser	
200 205	
Leu Lys Lys Val Pro Glu Lys Met Val Val Ile Gly Ala Gly Val Ile	
210 215 220	
Gly Val Glu Leu Gly Ser Val Trp Gln Arg Leu Gly Ala Asp Val Thr	
225 230 235 240	
Ala Val Glu Phe Leu Gly His Val Gly Gly Val Gly Ile Asp Met Glu	
276	

15 Glu Gly Ile Ile Cys Val Glu Gly Met Ala Gly Gly Ala Val His Ile

Asp Tyr Asn Cys Val Pro Ser Val Ile Tyr Thr His Pro Glu Val Ala

Trp Val Gly Lys Ser Glu Glu Gln Leu Lys Glu Glu Gly Ile Glu Tyr

Lys Val Gly Lys Phe Pro Phe Ala Ala Asn Ser Arg Ala Lys Thr Asn

ឧ

Ala Asp Thr Asp Gly Met Val Lys Ile Leu Gly Gln Lys Ser Thr Asp

Ile Gly Asp Val Val Ala Gly Pro Met Leu Ala His Lys Ala Glu Asp

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rie Ser Lys Asn Phe Gin Arg lie Leu Gin Lys Gin Gly Phe Lys Phe

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Lys Leu Asn Thr Lys Val Thr Gly Ala Thr Lys Lys Ser Asp Gly Lys

. 265

5 Ile Asp Val Ser Ile Glu Ala Ala Ser Gly Gly Lys Ala Glu Val Ile

Thr Cys Asp Val Leu Leu Val Cys Ile Gly Arg Arg Pro Phe Thr Lys

Asn Leu Gly Leu Glu Glu Leu Gly Ile Glu Leu Asp Pro Arg Gly Arg

lle Pro Val Asn Thr Arg Phe Gln Thr Lys Ile Pro Asn Ile Tyr Ala

a Glu Lys Arg Gly 40 7 Pro Lys Ala Leu 55
40 Leu Asn Arg Pro Lys Ala Leu Asn Ala Leu Cys Asp Gly 55 60 31u Leu Asn Gln Ala Leu Lys Ile Phe Glu Glu Asp Pro
Leu Asn Arg Pro Lys Ala Leu Asn Ala Leu Cys Asp Gly 55 60 3lu Leu Asn Gln Ala Leu Lys Ile Phe Glu Glu Asp Pro
55 31u Leu Asn Gln Ala Leu Lys Ile Phe Glu Glu Asp Pro
Slu Leu Asn Gln Ala Leu Lys Ile Phe Glu Glu Asp Pro
70 75 80
Ala Val Gly Ala Ile Val Leu Thr Gly Gly Asp Lys Ala Phe Ala Ala
85 90 95
Gly Ala Asp Ile Lys Glu Met Gln Asn Leu Ser Phe Gln Asp Cys Tyr
100 105 110
Ser Ser Lys Phe Leu Lys His Trp Asp His Leu Thr Gln Val Lys Lys
120.
Pro Val Ile Ala Ala Val Asn Gly Tyr Ala Phe Gly Gly Gly Cys Glu
135
Leu Ala Met Met Cys Asp Ile Ile Tyr Ala Gly Glu Lys Ala Gln Phe
150 155 160
Ala Gin Pro Glu ile Leu ile Gly Thr ile Pro Gly Ala Gly Gly Thr
165 170 175
Gin Arg ieu Thr Arg Ala Val Gly Lys Ser Leu Ala Met Glu Met Val
180 185 190
Leu Thr Gly Asp Arg Ile Ser Ala Gln Asp Ala Lys Gln Ala Gly Leu
200 . 205
Val Ser Lys Ile Cys Pro Val Glu Thr Leu Val Glu Glu Ala Ile Gln
215 220
Ala Ile Val Leu Ale Lius Glu Met (100 Phe Leu Lys His Phe Leu Cys Asp Ile 1150 Hr Arg Ala Val (165 Pro Val (167 Pro Val (1

WO 2004/055519 PCT/EP2003/014057	7501	WO 2004/055519	5519 124/335	PCT/EP2003/014057
Cys Ala Glu Lys Ile Ala Ser Asn Ser Lys Ile Val Val Ala Met Ala		Ala Pro	Ala Pro Leu Pro Gly Leu Ser Ala Pro Gly Arg Leu Phe Asp Gln Arg	he Asp Gln Ara
225 230 . 235 . 240	·		20 25	30
Lys Glu Ser Val Asn Ala Ala Phe Glu Met Thr Leu Thr Glu Gly Ser		Phe Gly	Phe Gly Glu Gly Leu Leu Glu Ala Glu Leu Ala Ala Leu Cys Pro Thr	eu Cys Pro Thr
245 250 255			35 40 . 45	
5 Lys Leu Glu Lys Lys Leu Phe Tyr Ser Thr Phe Ala Thr Asp Asp Arg		5 Thr Leu	Thr Leu Ala Pro Tyr Tyr Leu Arg Ala Pro Ser Val Ala Leu Pro Val	la Leu Pro Val
. 260 265 270		. 20	. 55	
Lys Glu Gly Met Thr Ala Phe Val Glu Lys Arg Lys Ala Asn Phe Lys		Ala Gln	Ala Gln Val Pro Thr Asp Pro Gly His Phe Ser Val Leu Leu Asp Val	sú Leu Asp Val
275 . 280 . 285			. 70	80
Asp Gln		Lys His	Lys His Phe Ser Pro Glu Glu Ile Ala Val Lys Val Val Gly Glu His	il Gly Glu His
10 290		. 01	88	
		Val Glu	Val Glu Val His Ala Arg His Glu Glu Arg Pro Asp Glu His Gly Phe	u His Gly Phe
			100 105	110
<210> 38		. Val Ala	Val Ala Arg Glu Phe His Arg Arg Tyr Arg Leu Pro Pro Gly Val Asp	o Gly Val Asp
<211> 160	٠		115 120 125	
15 <212> PRT	ŧ	15 Pro Ala	Pro Ala Ala Val Thr Ser Ala Leu Ser Pro Glu Gly Val Leu Ser Ile	l Leu Ser Ile
<213> Homo sapiens		130	135 140	
<220>		Gln Ala 2	Gin Ala Ala Pro Ala Ser Ala Gin Ala Pro Pro Pro Ala Ala Ala Lys	a Ala Ala Lye
<221> Heat-shock 20 kDa like-protein p20	•	145	150 . 155	160
<222> (1)(160)				
20 <223> Accession No. as of 09 Dec 2002: 014558		20		
<400> 38		<210> 39		
		<211> 151	д	
Met Glu ile Pro Val Pro Val Gln Pro Ser Trp Leu Arg Arg Ala Ser		<212> PRT		
1 5 10 15		<213> Ho	Homo sapiens	

>	WO 2004/055519	PCT/EP2003/014057	WO 2004/05519	PCT/EP2003/014057
	•			
	<220>		Val Arg His Ile Leu Ser Gly	
	<221> Myosin light chain alkali, non-muscle isoform	form	145 150	
	<222> (1)(151)			
	<223> Accession No. as of 09 Dec 2002: P16475			
8	<400> 39		5 <210> 40	
		• .	<211> 592	
	Met Cys Asp Phe Thr Glu Asp Gln Thr Ala Glu Phe Lys	Lys Glu Ala Phe	-212> PRT	
	1 5 10	15	<213> Ното вартеня	
	Gln Leu Phe Asp Arg Thr Gly Asp Gly Lys Ile Leu Tyr	lyr Ser Gln Cys	<220>	
10	. 25	. 02	10 <221> Calnexin precursor	
	Gly Asp Val Met Arg Ala Leu Gly Gln Asn Pro Thr Asn	Asn Ala Glu Val	<222> (1)(592)	
	3.5	45	<223> Accession No. as of 09 Dec 2002; P27824	
	Leu Lys Val Leu Gly Asn Pro Lys Ser Asp Glu Met Asn Val Lys Val	Asn Val Lys Val	<400> 40	
	50 55 60			
15	Leu Asp Phe Glu His Phe Leu Pro Met Leu Gln Thr Val	Al Ala Lys Asn	15 Met Glu Gly Lys Trp Leu Leu Cys Met Leu Leu Val Leu Gly Thr Ala	. Thr Ala
	65 70 . 75	08 ·	. 1 5 10	15
	Lys Asp Gln Gly Thr Tyr Glu Asp Tyr Val Glu Gly Leu Arg Val Phe	eu Arg Val Phe	ile Val Glu Ala His Asp Gly His Asp Asp Asp Val Ile Asp Ile Glu	Ile Glu
	95	56	. 20 25 30	
-	Asp Lys Glu Gly Asn Gly Thr Val Met Gly Ala Glu Ile Arg His Val	le Arg His Val	Asp Asp Leu Asp Asp Val Ile Glu Glu Val Glu Asp Ser Lys Pro Asp	Pro Asp
70	100 105	110	20 . 35 40 45	٠
	Leu Val Thr Leu Gly Glu Lys Met Thr Glu Glu Glu Val Glu Met Leu	al Glu Met Leu	Thr Thr Ala Pro Pro Ser Ser Pro Lys Val Thr Tyr Lys Ala Pro Val	Pro Val
	115 120 1	125		
_	Val Ala Gly His Glu Asp Ser Asn Gly Cys Ile Asn Tyr Glu Ala Phe	yr Glu Ala Phe	Pro Thr Gly Glu Val Tyr Phe Ala Asp Ser Phe Asp Arg Gly Thr Leu	Thr Leu
	130 135 . 140		65 70 75	80

WO 2004/055519	127/33\$	PCT/EP2003/014057	. WO 2004/055519	PCT/EP2003/0:
Ser Gly Trp Ile Leu Ser Lys Ala Lys Lys Asp Asp Thr Asp Asp Glu	a Lys Lys Asp Asp Thr As	p Asp Glu	Ser Arg Glu Ile Glu Asp Pro	Ser Arg Glu ile Glu Asp Pro Glu Asp Arg Lye Pro Glu Asp Trp Asp
85	06	8	275	280 285
Ile Ala Lys Tyr Asp Gly Lys Trp Glu Val Glu Glu Met Lys Glu Ser	o Giu Val Glu Glu Met Ly	s Glu Ser	Glu Arg Pro Lys Ile Pro Asp	Glu Arg Pro Lys Ile Pro Asp Pro Glu Ala Val Lys Pro Asp Asp Trp
100	105 110	0	290 295	300
5 Lys Leu Pro Gly Asp Lys Gly Leu Val Leu Met Ser Arg Ala Lys	ı Val Leu Met Ser Arg Alı	a Lys His	Asp Glu Asp Ala Pro Ala Lys	Asp Glu Asp Ala Fro Ala Lys Ile Pro Asp Glu Glu Ala Thr Lys Pro
115 120	125		305 310	315 320
His Ala Ile Ser Ala Lys Leu Asn Lys Pro Phe Leu Phe Asp Thr Lys	1 Lys Pro Phe Leu Phe Asy	p Thr Lys	Glu Gly Trp. Leu Asp Asp Glu	Glu Gly frp. Leu Asp Asp Glu Pro Glu Tyr Val Pro Asp Pro Asp Ala
130 135	. 140		325	330 335
Pro Leu 11e Val Gln Tyr Glu Val Asn Phe Gln Asn Gly Ile Glu Cys	. Asn Phe Gln Asn Gly Ile	e Glu Cys	Glu Lys Pro Glu Asp Trp Asp	Glu Lys Pro Glu Asp Trp Asp Glu Asp Met Asp Gly Glu Trp Glu Ala
10 145 150	. 155	160	. 340	345 350
Gly Gly Ala Tyr Val Lys Leu Leu Ser Lys Thr Pro Glu Leu Asn Leu	. Ser Lys Thr Pro Glu Le	u Asn Leu	Pro Gln Ile Ala Asn Pro Arg	Pro Gln Ile Ala Asn Pro Arg Cys Glu Ser Ala Pro Gly Cys Gly Val
165	170	175	355	360 365
Asp Gin Phe His Asp Lys Thr Pro Tyr Thr Ile Met Phe Gly Pro Asp	Tyr Thr Ile Met Phe Gly	y Pro Asp	Trp Gln Arg Pro Val 11e Asp	Trp Gln Arg Pro Val 11e Asp Asn Pro Asn Tyr Lys Gly Lys Trp Lys
180	185 190	8	370 375	380
is Lys Cys Gly Glu Asp Tyr Lys Leu His Phe Ile Pi	His Phe Ile Phe Arg His Lys Asn	s Lys Asn . 15	Pro Pro Met Ile Asp Asn Pro	Pro Pro Met 11e Asp Asn Pro Ser Tyr Gln Gly 11e Trp Lys Pro Arg
195 200	205		385 . 390	395 400
Pro Lys Thr Gly Ile Tyr Glu Glu Lys His. Ala Lys Arg Pro Asp Ala	Lys His.Ala Lys Arg Pro	о Авр Ала	Lys Ile Pro Asn Pro Asp Phe	Lys Ile Pro Asn Pro Asp Phe Phe Glu Asp Leu Glu Pro Phe Arg Met
210 215	220		405	410 415
Asp Leu Lys Thr Tyr Phe Thr Asp Lys Lys Thr His Leu Tyr Thr Leu	Lys Lys Thr His Leu Tyr	r Thr Leu	Thr Pro Phe Ser Ala Ile Gly	Thr Pro Phe Ser Ala Ile Gly Leu Glu Leu Trp Ser Met Thr Ser Asp
20 225 . 230	235	340	420	425 430
lle Leu Asn Pro Asp Asn Ser Phe Glu Ile Leu Ve	Glu ile Leu Val Asp Gln Ser Val	ser Val	Ile Phe Phe Asp Asn Phe Ile 1	ile Phe Phe Asp Asn Phe ile ile Cys Ala Asp Arg Arg ile Val Asp
245	250	255	435	440 445
Val Asm Ser Gly Asm Leu Leu Asm Asp Met Thr Pro Pro Val Asm Pro	Asp Met Thr Pro Pro Val		Asp Trp Ala Asn Asp Gly Trp G	Asp Trp Ala Asn Asp Gly Trp Gly Leu Lys Lys Ala Ala Asp Gly Ala
260	265 270		450 455	460

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Ala Glu Pro Gly Val Val Gly Gln Met Ile Glu Ala Ala Glu Glu Arg	<222> (1)(282)
465 470 475 480	<223> Accession No. as of 09 Dec 2002: Q07021
Pro Trp Leu Trp Val Val Tyr Ile Leu Thr Val Ala Leu Pro Val Phe	<400> 41
485 490 495	
Leu Val Ile Leu Phe Cys Cys Ser Gly Lys Lys Gln Thr Ser Gly Met	Met Leu Pro Leu Leu Arg Cys Val Pro Arg Val Leu Gly Ser Ser Val
500 505 510	1 5 10 15
Glu Tyr Lys Lys Thr Asp Ala Pro Gln Pro Asp Val Lys Glu Glu Glu	Ala Gly Leu Arg Ala Ala Aro Ala Ser Pro Phe Arg Gln Leu Leu
515 520 525	20 25 30
Glu Glu Lys Glu Glu Glu Lys Asp Lys Gly Asp Glu Glu Glu Glu Gly	Gln Pro Ala Pro Arg Leu Cys Thr Arg Pro Phe Gly Leu Leu Ser Val
530 535 540	35 40
Glu Glu Lys Leu Glu Glu Lys Gln Lys Ser Asp Ala Glu Glu Asp Gly	Arg Ala Gly Ser Glu Arg Arg Pro Gly Leu Leu Arg Pro Arg Gly Pro
545 550 550	90 25 60
Gly Thr Val Ser Gin Glu Glu Glu Asp Arg Lys Pro Lys Ala Glu Glu	Cys Ala Cys Gly Cys Gly Ser Leu His Thr Asp Gly Asp Lys
565 570 575	65 70 75 80
15 Asp Glu Ile Leu Asn Arg Ser Pro Arg Asn Arg Lys Pro Arg Arg Glu	Ala Phe Val Asp Phe Leu Ser Asp Glu Ile Lys Glu Glu Arg Lys Ile
	85 90 95
	Gln Lys His Lys Thr Leu Pro Lys Met Ser Gly Gly Trp Glu Leu Glu
	100 105 110
<210> 41	Leu Asn Gly Thr Glu Ala Lys Leu Val Arg Lys Val Ala Gly Glu Lys
<211.> 282 20	115 120 1.25
<212> PRT	ile Thr Val Thr Phe Asn Ile Asn Asn Ser Ile Pro Pro Thr Phe Asp
<213> Homo sapiens	130 135 140
<2220>	Gly Glu Glu Glu Pro Ser Gln Gly Gln Lys Val Glu Glu Gln Glu Pro
<221> Complement component 1	145 150 155 160

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WO 2004/055519 PCT/EP2003/014057	WO 2004/055519 PCT/EP2	PCT/EP2003/01
Glu Leu Thr Ser Thr Pro Agn Phe Val Val Glu Val 11e Lys Agn Asp	precursor	
165 170 175	<222> (1)(727)	
Asp Gly Lys Lys Ala Leu Val Leu Asp Cys His Tyr Pro Glu Asp Glu	<223> Accession No. as of 09 Dec 2002: P28331	
180 185 190	<400> 42	
5 Val Gly Glu Asp Glu Ala Glu Ser Asp Ile Phe Ser Ile Arg Glu	un.	
195 200 205	Met Leu Arg Ile Pro Val Arg Arg Ala Leu Val Gly Leu Ser Lys Ser	's Ser
Val Ser Phe Gln Ser Thr Gly Glu Ser Glu Trp Lys Asp Thr Asn Tyr	1 5 10 15	
210 215 220	. Pro Lys Gly Cys Val Arg Thr Thr Ala Thr Ala Ala Ser Asn Leu Ile	u Ile
Thr Leu Asn Thr Asp Ser Leu Asp Trp Ala Leu Tyr Asp His Leu Met	20 25 30	
) 225 230 235 240	10 Glu Val Phe Val Asp Gly Gln Ser Val Met Val Glu Pro Gly Thr Thr	r Thr
Asp Phe Leu Ala Asp Arg Gly Val Asp Asn Thr Phe Ala Asp Glu Leu	35	•
245 250 255	Val Leu Gln Ala Cys Glu Lys Val Gly Met Gln Ile Pro Arg Phe Cys	e Cys
Val Glu Leu Ser Thr Ala Leu Glu His Gln Glu Tyr 11e Thr Phe Leu	9 55 . 05	
260 265 270	Tyr His Glu Arg Leu Ser Val Ala Gly Asn Cys Arg Met Cys Leu Val	u Val
Glu Asp Leu Lys Ser Phe Val Lys Ser Gln	15 65 70 75 80	. 08
275 280	Glu ile Glu Lys Ala Pro Lys Val Val Ala Ala Cys Ala Met Pro Val	o Val
	85 90	
	Met Lys Gly Trp Asn Ile Leu Thr Asn Ser Glu Lys Ser Lys Lys Ala	s Ala
<21.0> 42	100 105 110	
<211> 727	20 Arg Glu Gly Val Met Glu Phe Leu Leu Ala Asn His Pro Leu Asp Cys	η. (γ
<212> PRT	115 120 125	
<213> Homo sapiens	Pro Ile Cys Asp Gln Gly Gly Glu Cys Asp Leu Gln Asp Gln Ser Met	: Met
<2220>	.130 135 140	
<221> NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	Met Phe Gly Asn Asp Arg Ser Arg Phe Leu Glu Gly Lys Arg Ala Val	. Val

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	WO 2004/055519 PCT/EP2003/014057 134/335	340 345 350	Ala Leu Lys Asp Leu Leu Asn Arg Val Asp Ser Asp Thr Leu Cys Thr	355 360 365	Glu Glu Val Phe Pro Thr Ala Gly Ala Gly Thr Asp Leu Arg Ser Asn	5 370 375 380	Tyr Leu Leu Asn Thr Thr Ile Ala Gly Val Glu Glu Ala Asp Val Val	385 390 395 400	Leu Leu Val Gly Thr Asn Pro Arg Phe Glu Ala Pro Leu Phe Asn Ala	. 405 410 415	10 .Trp Ile Arg Lys Ser Trp Leu His Asn Asp Leu Lys Val Ala Leu Ile	420 425 430	Gly Ser Pro Val Asp Leu Thr Tyr Thr Tyr Asp His Leu Gly Asp Ser	435 440 445	Pro Lys Ile Leu Gln Asp Ile Ala Ser Gly Ser His Pro Phe Ser Gln	15 450 455 460	Val Leu Lys Glu Ala Lys Lys Pro Met Val Val Leu Gly Ser Ser Ala	465 470 475 . 480	. Leu Gln Arg Asn Asp Gly Ala Ala Ile Leu Ala Ala Val Ser Ser Ile	485 490 . 495	20 Ale Gin Lys Ile Arg Met Thr Ser Gly Val Thr Gly Asp Trp Lys Val	500 505 510	Met Asn ile Leu His Arg Ile Ala Ser Gln Val Ala Ala Leu Asp Leu	515 520 525	Gly Tyr Lys Pro Gly Val Glu Ala Ile Arg Lys Asn Pro Pro Lys Val			
· .	1057																											
	WO 2004/055519 PCT/EP2003/014057 133/335	145 150 155. 160	Glu Asp Lys Asn Ile Gly Pro Leu Val Lys Thr Ile Met Thr Arg Cys	165 170 7 175	lle Gln Cys Thr Arg Cys Ile Arg Phe Ala Ser Glu Ile Ala Gly Val	5 180 185 190	Asp Asp Leu Gly Thr Thr Gly Arg Gly Asn Asp Met Gln Val Gly Thr	195 200 205	Tyr lle Glu Lys Met Phe Met Ser Glu Leu Ser Gly Asn Ile Ile Asp	210 215 220	10 Ile Cys Pro Val Gly Ala Leu Thr Ser Lys Pro Tyr Ala Phe Thr Ala	225 230 235 240	Arg Pro Trp Glu Thr Arg Lys Thr Glu Ser Ile Asp Val Met Asp Ala	245 250 255	Val Gly Ser Asn Ile Val Val Ser Thr Arg Thr Gly Glu Val Met Arg	15 260 265 270	ile Leu Pro Arg Met His Glu Asp ile Asn Glu Glu Trp ile Ser Asp	275 280 285	Lys Thr Arg Phe Ala Tyr Asp Gly Leu Lys Arg Gln Arg Leu Thr Glu	290 295 300	20 Pro Met Val Arg Asn Glu Lys Gly Leu Leu Thr Tyr Thr Ser Trp Glu	305 310 315 320	Asp Ala Leu Ser Arg Val Ala Gly Met Leu Gln Ser Phe Gln Gly Lys	325 330 335	Asp Val Ala Ala Ile Ala Gly Gly Leu Val Asp Ala Glu Ala Leu Val			
										•								•									•	

	WO 2004/055519	135/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/0
	530 535	540		725
	Leu Phe Leu Leu Gly Ala Asp Gly Gly Cys Ile		Thr Arg Gln Asp Leu	
	545 550	555	960	
	Pro Lys Asp Cys Phe 11e 11e Tyr Gln Gly His His Gly Asp Val Gly	Tyr Gln Gly Kis His Gly	Asp Val Gly	<210> 43
ιn		570	575	5 <211> 491
	Ale Pro Ile Ala Asp Val Ile Leu Pro Gly Ala Ala Ty $oldsymbol{x}$ Thr Glu Lys	Leu Pro Gly Ala Ala Tyr	Thr Glu Lys	<212> PRT
	580	585	290	<213> Homo sapiens
	Ser Ala Thr fyr Val Asn Thr Glu Gly Arg Ala Gln Gln Thr Lys Val	Glu Gly Arg Ala Gln Gln	Thr Lys Val	<22.0>
	595	600 605		<221> Pre-B cell enhancing factor precursor
01	Ala Val Thr Pro Pro Gly Leu Ala Arg Glu Asp Trp Lys Ile Ile Arg	Ala Arg Glu Asp Trp Lys	ile ile Arg	10 <222> (1)(491)
	, 610 , 615	620		<223> Accession No. as of 09 Dec 2002; P43490
	Ala Leu Ser Glu ile Ala Gly Met Thr Leu Pro Tyr Asp Thr Leu Asp	Met Thr Leu Pro Tyr Asp	Thr Leu Asp	<400> 43
	625 630	635	640	
	Gln Val. Arg Asn Arg Leu Glu Glu Phe Ser Pro Asn Leu Val Arg Tyr	3lu Phe Ser Pro Asn Leu	Val Arg Tyr	Met Asn Pro Ala Ala Glu Ala Glu Phe Asn Ile Leu Leu Ala Thr Asp
15	645	650	655	15 1 5 10 15
	Asp Asp Ile Glu Gly Ala Asn Tyr Phe Gln Gln Ala Asn Glu Leu Ser	lyr Phe Gln Gln Ala Asn	Glu beu Ser	Ser Tyr Lys Val Thr His Tyr Lys Gln Tyr Pro Pro Asn Thr Ser Lys
	099		670	20 25 30
	Lys Leu Val Asn Gin Gin Leu Leu Ala Asp Pro Leu Val Pro Pro Gin	eu Ala Asp Pro Leu Val	Pro Pro Gln	Val Tyr Ser Tyr Phe Glu Cys Arg Glu Lys Lys Thr Glu Asn Ser Lys
	675	680 685		35 40 45
20	Leu Thr Leu Lys Asp Phe Tyr Met Thr Asp Ser Ile Ser Arg Ala Ser	et Thr Asp Ser Ile Ser	Arg Ala Ser	20 Leu Arg Lys Val Lys Tyr Glu Glu Thr Val Phe Tyr Gly Leu Gln Tyr
	690 695	700		09 . 55 05
	Gln Thr Met Ala Lys Cys Val Lys Ala Val Thr Gl	ys Ala Val Thr Glu Gly	u Gly Ala Gln Ala	ile Leu Asn Lys Tyr Leu Lys Gly Lys Val Val Thr Lys Glu Lys Ile
	705 710	715.	720	65 70 . 75 80
	Val Glu Glu Pro Ser Ile Cys			Gln Glu Ala Lys Asp Val Tyz Lys Glu His Phe Gln Asp Asp Val Phe

014057 WO 2004/055519 PCT/EP2003/0:	275 280 285	Lys Ile Trp Gly Glu Asp Leu Arg His Leu Ile Val Ser Arg Ser Thr	290 295 300	Gin Ala Pro Leu ile ile Arg Pro Asp Ser Gly Asn Pro Leu Asp Thr	5 305 310 315	Val Leu Lys Val Leu Glu Ile Leu Gly Lys Lys Phe Pro Val Thr Glu	325 330 335	Asn Ser Lys Gly Tyr Lys Leu Leu Pro Pro Tyr Leu Arg Val Ile Gln	340 345 350	10 Gly Asp Gly Val Asp Ile Asn Thr Leu Gln Glu Ile Val Glu Gly Met	355 360	Lys Gln Lys Met Trp Ser Ile Glu Asn Ile Ala Phe Gly Ser Gly Gly	370 375 380	Gly Leu Leu Gln Lys Leu Thr Arg Asp Leu Leu Asn Cys Ser Phe Lys	395 390 395	Cys Ser Tyr Val Val Thr Asn Gly Leu Gly Ile Asn Val Phe Lys Asp	405 410 415	Pro Val Ala Asp Pro Asn Lys Arg Ser Lys Lys Gly Arg Leu Ser Leu	420 425 430	20 His Arg Thr Pro Ala Gly Asn Phe Val Thr Leu Glu Glu Gly Lys Gly	435 440 445	Asp Leu Glu Glu Tyr Gly Gin Asp Leu His Thr Vel Phe Lys Asn	:
PCT/EP2003/014057	95	s Tyr Asp Gly His Leu	110	Pro Ile Glu Ile Lys Ala Val Pro Glu Gly Phe Val Ile Pro Arg Gly	125	Asn Val Leu Phe Thr Val Glu Asn Thr Asp Pro Glu Cys Tyr Trp Leu	140	Trp Tyr Pro Ile Thr	160	i Leu Ala Lys Tyr Leu	. 175	Tyr Lys Leu His Asp	190	Ala Gly Ile Gly Ala	205	Thr Val Ala Gly Leu	220	Pro Val Pro Gly Tyr	240	Ala Trp Gly Lys Asp	255	Gln Phe Ser Ser Val	c c
137/335	06	Asn Glu Lys Gly Trp Asn Tyr Ile Leu Glu Lys Tyr Asp Gly His	105	a Val Pro Glu Gly Phe	120	l Glu Asn Thr Asp Pro	135	Thr Asn Trp lle Glu Thr Ile Leu Val Gln Ser Trp Tyr Pro Ile Thr	0 155	Val Ala Thr Asn Ser Arg Glu Gln Lys Lys Ile Leu Ala Lys	170	Leu Glu Thr Ser Gly Asn Leu Asp Gly Leu Glu Ty	185	Phe Gly Tyr Arg Gly Vel Ser Ser Gln Glu Thr Ala Gly Ile Gly Ala	200	Ser Ala His Leu Val Asn Phe Lys Gly Thr Asp Thr Vel Ala Gly Leu	215	Ala Leu ile Lys Lys Tyr Gly Thr Lys Asp Pro Val Pro Gly	235	Ser Val Pro Ale Ala Glu His Ser Thr Ile Thr Ala	250	His Glu Lys Asp Ala Phe Glu His Ile Val Thr Gln Phe Ser Ser Val	265
WO 2004/055519	85	Lys Gly Trp As	100	Glu Ile Lys Al	115	Leu Phe Thr Val		Trp Ile Glu Thi	150	Thr Asn Ser Arg	165	Thr Ser Gly Asn	180	Iyr Arg Gly Val	195	His Leu Val Asn		ile Lys Lys Tyr	230	Pro Ala Ala Glu	245	ys Asp Ala Phe	260

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465 470 475 480 Gin Leu Am Ile Glu Leu Glu Ala Ala His His 490 Glin Leu Am Ile Glu Leu Glu Ala Ala His His 490 4210 44 4211> 135 4212 PRT 421 4222 (1)(135) 4222 (1)(135) 4224 (1)(135) 4225 (1)(135) 4226 (1)(135) 423 Accession No. as of 09 Dec 2002; prop455 4200 44 Het Pro Val Amp Phe Thr Gly Tyr Typ Lyg Met Leu Val Amn Glu Asn 15 Phe Glu Glu Tyr Leu Ary Ala Leu Amp Val Asn Fuy And Leu Arg Lyg 20 23 30 11e Ala Asn Leu Leu Lyg Pro App Lyg Glu Ile Val Gln Asp Gly Asp 35 40 45 Hid Met Ile Ile Arg Thr Leu Ser Thr Phe Arg Asn Tyr Ile Met Asp Asp 50 56 Phe Gln Val Gly Lyg Glu Dhe Glu Glu Asp Leu Thr Gly Ile Asp Asp Phe Gln Val Gly Lyg Glu Dhe Glu Glu Asp Leu Thr Gly Ile Asp Asp	WO 2004/055519 PCT/EP2003/014057 140/335	65 70 75 80	Arg Lys Cys Met Thr Thr Val Ser Trp Asp Gly Asp Lys Leu Gln Cys	 Val Gln Lys Gly Glu Lys Glu Gly Arg Gly Trp Thr Gln Trp Ile Glu	5 100 105 110	Gly Asp Glu Leu His Leu Glu Met Arg Val Glụ Gly Val Val Cys Lys	115 120 125	Gin Vel Phe Lys Lys Val Gin	130 135	01		<210> 45	<211> 544	<212> PRT	15 <213> Homo sapiens	<220>	<221> T-complex protein 1, gamma subunit	<222> (1)(544) "	<223> Accession No. as of 09 Dec 2002: P49368	20 <400> 45		Met Gly His Arg Pro Val Leu Val Leu Ser Gln Asn Thr Lys Arg Glu	. 1 5 10 15	Ser Gly Arg Lys Val Gln Ser Gly Asn lle Asn Ala Ala Lys Thr Ile	
470 470 475 Asn Ile Glu Leu Glu Ala Ala His His 485 490 485 490 35 35 36 37 37 37 38 38 39 39 39 39 39 39 39 30 30 30 30 30 30 30 30 30 30 30 30 30	PCT/EP2003/014057	480												•		Val Asn Glu Asn	15	Ala Leu Arg Lys	30	Gln Asp Gly Asp		lyr ile Met Asp		sly Lie Asp Asp	
			Asn Ile Glu Leu Glu Ala Ala His His				35	ŲT.	ото sapiens		tinol-binding protein I, cellular	.) (135)	cession No. as of 09 Dec 2002; P09455			al Asp Phe Thr Gly Tyr Trp Lys Met Leu		lu Tyr Leu Arg Ala Leu Asp Val Asn Val A		sn Leu Leu Lys Pro Asp Lys Glu Ile Val G	40	le ile Arg Thr Leu Ser Thr Phe Arg Asn T		il Gly Lys Glu Phe Glu Glu Asp Leu Thr G	

WO 2004/055519	PCT/EP2003/014057	WO 1004/055519 PCT	PCT/EP2003/014057
		On age	
20	25 30	210 215 220	
Ala Asp Ile Ile Arg Thr Cys Leu Gly Pro Lys Ser Met	Gly Pro Lys Ser Met Met Lys Met	His Pro Arg Met Arg Tyr Ile Lys Asn Pro Arg Ile Val Leu Leu	nen ner
35 40	45	. 225 . 230 . 235	240
Leu Leu Asp Pro Met Gly Gly Ile Val Met Thr Asn Asp	Val Met Thr Asn Asp Gly Asn Ala	Asp Ser Ser Leu Glu Tyr Lys Lys Gly Glu Ser Gln Thr Asp Ile Glu	ile Glu
5 50 55	· · · · · · · · · · · · · · · · · · ·	. 245 250	255
Ile Leu Arg Glu Ile Gln Val Gln His Pro Ala Ala Lys	His Pro Ala Ala Lys Ser Met Ile	Ile Thr Arg Glu Glu Asp Phe Thr Arg Ile Leu Gln Met Glu Glu Glu	ilu Glu
65 70	75 80	260 265 270	
Glu Ile Ser Arg Thr Gln Asp Glu Glu Val Gly Asp Gly	Glu Val Gly Asp Gly Thr Thr Ser	Tyr ile Gin Gin Leu Cys Glu Asp ile ile Gin Leu Lys Pro Asp Val	ap val
58 .		. 275 280 285	
10 Val Ile Ile Leu Ala Gly Glu Met Leu Ser Val Ala Glu His Phe Leu	Leu Ser Val Ala Glu His Phe Leu	Val Ile Thr Glu Lys Gly Ile Ser Asp Leu Ala Gln His Tyr Leu Met	eu Met
. 100	105	290 295 300	
Glu Gln Gln Met Hie Pro Thr Val Val Ile Ser Ala Tyr Arg Lys Ala	Val Ile Ser Ala Tyr Arg Lys Ala	Arg Ala Asn 11e Thr Ala 11e Arg Arg Val Arg Lys Thr Asp Asn Asn	sn Asn
115 120	125	305 310 315	320
Leu Asp Asp Met Ile Ser Thr Leu Lys Lys Ile Ser Ile Pro Val Asp	Lys Lys Ile Ser Ile Pro Val Asp	Arg Ile Ala Arg Ala Cys Gly Ala Arg Ile Val Ser Arg Pro Glu Glu	lu Glu
15 130 135	140 15	325 330 335	35
Ile Ser Asp Ser Asp Met Met Leu Asn Ile Ile Asn Ser S	Asn ile ile Asn Ser Ser Ile Thr	Leu Arg Glu Asp Asp Val Gly Thr Gly Ala Gly Leu Leu Glu Ile Lys	lе <i>L</i> ув
145 150	155 160	340 345 350	
Thr Lys Ala Ile Ser Arg Trp Ser Ser Leu Ala Cys Asn Ile Ala Leu	Ser Leu Ala Cys Asn Ile Ala Leu	Lys ile Gly Asp Glu Tyr Phe Thr Phe ile Thr Asp Cys Lys Asp Pro	p Pro
165	170	355 360 365	
20 Asp Ala Val Lys Met Val Gin Phe Glu Glu Asn Gly Arg Lys Glu Ile	3lu Glu Asn Gly Arg Lys Glu Ile	Lys Ala Cys Thr Ile Leu Leu Arg Gly Ala Ser Lys Glu Ile Leu	u Ser
180	185 190	370 375 380	
Asp lle Lys Lys Tyr Ala Arg Val Glu Lys Ile Pro Gly Gly Ile	ilu Lys Ile Pro Gly Gly Ile Ile .	Glu Val Glu Arg Asn Leu Gln Asp Ala Met Gln Val Cys Arg Asn Val	m Val
195 200		385 390 395	400
Glu Asp Ser Cys Val Leu Arg Gly Val Met Ile Asn Lys Asp Val Thr	al Met ile Asn Lys Asp Val Thr	Leu Leu Asp Pro Gin Leu Val Pro Gly Gly Gly Ala Ser Glu Met Ala	t Ala

	WO 2004/055519 PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057 144/335
	405 410 415	<221> Placental ribonuclease inhibitor
	Val Ala His Ala Leu Thr Glu Lys Ser Lys Ala Met Thr Gly Val Glu	<222> (1)(461)
•	420 425 430 -	<223> Accession No. as of 09 Dec 2002: 213489
	Gln Trp Pro Tyr Arg Ale Val Ale Gln Ale Leu Glu Vel Ile Pro Arg	<400> 46
.v.	435 440 445 5	
	Thr Leu Ile Gln Asn Cys Gly Ala Ser Thr Ile Arg Leu Leu Thr Ser	Met Ser Leu Asp ile Gln Ser Leu Asp Ile Gln Cys Glu Glu Leu Ser
	450 . 455 . 460	1 5 10 15
	Leu Arg Ala Lys His Thr Gln Glu Asn Cys Glu Thr Trp Gly Val Asn	Asp Ala Arg Trp Ala Glu Leu Leu Pro Leu Leu Gln Gln Cys Gln Val
	465 . 470 . 475 480	20 25 30
2	10 Gly Glu Thr Gly Thr Leu Val Asp Met Lys Glu Leu Gly Ile Trp Glu	Val Arg Leu Asp Asp Cys Gly Leu Thr Glu Ala Arg Cys Lys Asp Ile
	485 490 495	35 40 45
	Pro Leu Ala Val Lys Leu Gln Thr Tyr Lys Thr Ala Val Glu Thr Ala	Ser Ser Ala Leu Arg Val Asn Pro Ala Leu Ala Glu Leu Asn Leu Arg
	500 505 510	50 55 60
	Val Leu Leu Leu Arg Ile Asp Asp Ile Val Ser Gly His Lys Lys Lys	Ser Asn Glu Leu Gly Asp Val Gly Val His Cys Val Leu Gln Gly Leu
15	515 520 525 15	65 70 75 80
	Gly Asp Asp Gln Ser Arg Gln Gly Gly Ala Pro Asp Ala Gly Gln Glu	Gin Thr Pro Ser Cys Lys Ile Gin Lys Leu Ser Leu Gin Asn Cys Cys
	530 535 540 .	56 06 _. 58
		Leu Thr Gly Ala Gly Cys Gly Val Leu Ser Ser Thr Leu Arg Thr Leu
		100 105 110
70	<210> 46	Pro Thr Leu Gln Glu Leu His Leu Ser Asp Asn Leu Gly Asp Ala
	<211> 461	115 120 .125
	<21.2> PRT	Gly Leu Gln Leu Leu Cys Glu Gly Leu Leu Asp Pro Gln Cys Arg Leu
	<213> Homo sapiens	130 135 140
	<2220>	Glu Lys Leu Glu Tyr Cys Ser Leu Ser Ala Ala Ser Cys Glu

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145 150 155 160	340 . 345 350
Pro Leu Ala Ser Val Leu Arg Ala Lys Pro Asp Phe Lys Glu Leu Thr	Leu Glu Asp Ala Gly Val Arg Glu Leu Cys Gln Gly Leu Gly Gln Pro
165 170 175	355 360 365
Val Ser Asn Asp Ile Asn Glu Ala Gly Val Arg Val Leu Cys Gln	Gly Ser Val Leu Arg Val Leu Trp Leu Ala Asp Cys Asp Val Ser Asp
5 180 185 , 190	5 370 375 380
Gly Leu Lys Asp Ser Pro Cys Gln Leu Glu Ala Leu Lys Leu Glu Ser	Ser Ser Cys Ser Leu Ala Ala Thr Leu Leu Ala Asn His Ser Leu
195 200 . 205	385 . 390 395 400
Cys Gly Val Thr Ser Asp Asn Cys Arg Asp Leu Cys Gly Ile Val Ala	Arg Glu Leu Asp Leu Ser Asn Asn Cys Leu Gly Asp Ala Gly Ile Leu
210 215 220	405 410 . 415
10 Ser Lys Ala Ser Leu Arg Glu Leu Ala Leu Gly Ser Asn Lys Leu Gly	10 Gln Leu Val Glu Ser Val Arg Gln Pro Gly Cys Leu Leu Glu Gln Leu
225 230 235 240	420 . 425 430
Asp Val Gly Met Ala Glu Leu Cys Pro Gly Leu Leu His Pro Ser Ser	Val Leu Tyr Asp Ile Tyr Trp Ser Glu Glu Met Glu Asp Arg Leu Gln
245 250 255	435 440 445
Arg Leu Arg Thr Leu Trp Ile Trp Glu Cys Gly Ile Thr Ala Lys Gly	Ala Leu Glu Lys Asp Lys Pro Ser Leu Arg Val Ile Ser
15 260 265 270	15 450 455 460
Cys Gly Asp Leu Cys Arg Val Leu Arg Ala Lys Glu Ser Leu Lys Glu	
275 280 285	
Leu Ser Leu Ala Gly Asn Glu Leu Gly Asp Glu Gly Ala Arg Leu Leu	<210> 47
290 . 295 . 300	<211> 317
20 Cys Glu Thr Leu Leu Glu Pro Gly Cys Gln Leu Glu Ser Leu Trp Val	20 <212> PRT
305 310 315 320.	<213> Homo maplens
Lys Ser Cys Ser Phe Thr Ala Ala Cys Cys Ser His Phe Ser Ser Val	<220>
325 330 335	<221> Guanine nucleotide-binding protein beta subunit-like protein
Leu Ala Gin Asn. Arg Phe Leu Ceu Glu Leu Gin Ile Ser Asn Asn Arg	12.3

	UI DE LE	
	147/335 FCITER 2003/01405/	WO 2004/055519 PCT/EP2003/0 148/335
-	<222> (1)(317)	Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val
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	<400> 47	Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr
		180
•,	5 Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly	5 Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala
	1. 5 10 . 15	195 200 205
	Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu	Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly
	20 . 25 . 30	210 215 220
	Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp	Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys
2	10 35 40 . 45	10 225 230 235 240
	Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His	Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile
	09. 25 05	245 250 255
	Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser	Lys 11e Trp Asp Leu Glu Gly Lys 11e 11e Val Asp Glu Leu Lys Gln
	65 70 75 80	260 265 270
15	15 Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Gly Thr	15 Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser
		275 280 285
	Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala	Leu Ale Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp
	100	290 295 300
	Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr	Asn Leu Val Arg Val Trp Gln Val Thr 11e Gly Thr Arg
70	20 115 120 125	20 305 310 315
	Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp	
	130 135 140	
	Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser	<210> 48
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	WO 2004/055519	PCT/EP2003/014057		WO 2004/055519	PCT/EP2003/014057
				150/333	
	<212> PRT			Thr Met Gly Asp Arg Phe Thr Asp Glu Glu Val Asp Glu Met Tyr Arg	Met Tyr Arg
	<213> Homo sapiens			. 130 135 140	
	<220>			Glu Ala Pro Ile Asp Lys Lys Gly Asn Phe Asn Tyr Val Glu Phe Thr	Glu Phe Thr
	<221> Myosin regulatory light chain 2	/ light chain 2		145 150 155	. 160
	5 <222> (1)(172)		, rv	Arg Ile Leu Lys His Gly Ala Lys Asp Lys Asp Asp	
	<223> Accession No. as	Accession No. as of 10 Dec 2002: P24844		165 170	
	<400> 48				
					-
	Met Ser Ser Lys Arg Ala	Met Ser Lys Arg Ala Lys Ala Lys Thr Thr Lys Lys Arg Pro Gln		<210> 49	
01	5 1 5	10 15	01	<211> 114	
	Arg Ala Thr Ser Asn Val	Arg Ala Thr Ser Asn Val Phe Ala Met Phe Asp Gln Ser Gln Ile Gln		<212> PRT	
	. 50	. 30		<213> Homo sepiens	
	Glu Phe Lys Glu Ala Phe	Glu Phe Lys Glu Ala Phe Asn Met Ile Asp Gln Asn Arg Asp Gly Phe		<2220>	
	. 35	40 45		<221> Calgranulin B	
15		ile Asp Lys Glu Asp Leu His Asp Met Leu Ala Ser Leu Gly Lys Asn	15	<2225 (1) (114)	
	05	55 60		<223> Accession No. as of 10 Dec 2002; P06702	
	Pro Thr Asp Glu Tyr Leu	Pro Thr Asp Glu Tyr Leu Glu Gly Met Met Ser Glu Ala Pro Gly Pro		<400> 49	
	65 70	75 80			
	Ile Asn Phe Thr Met Phe	Ile Asn Phe Thr Met Phe Leu Thr Met Phe Gly Glu Lys Leu Asn Gly		Met Thr Cys Lys Met Ser Gln Leu Glu Arg Asn Ile Glu Thr Ile Ile	Thr Ile Ile
20	882	90 95	20		15
	Thr Asp Pro Glu Asp Val	Thr Asp Pro Glu Asp Val Ile Arg Asn Ala Phe Ala Cys Phe Asp Glu		Asn Thr Phe His Gin Tyr Ser Val Lys Leu Gly His Pro Asp Thr Leu	Asp Thr Leu
	100	105		20 25	30
	Glu Ala Ser Gly Phe Ile	Glu Ala Ser Gly Phe Ile His Glu Asp His Leu Arg Glu Leu Leu Thr		Asn Gln Gly Glu Phe Lys Glu Leu Val Arg Lys Asp Leu Gln Asn Phe	Gln Asn Phe
	115	120 125		35 . 40 45	

W	WO 2004/055519	151/335	PCT/EP2003/014057	25	WO 2004/055519 152/335	PCT/EP2003/014057
•						
ភ័	Leu Lys Lys Glu Asn Lys Asn Glu Lys Val Ile Glu Hi	Asn Glu Lys Val Ile G	ilu His Ile Met Glu		Gin Asp Pro Gly Leu His Val Trp Arg Val Glu Lys Leu Lys Pro Val	Glu Lys Leu Lys Pro Val
	50	55 6	09		20 25	30
ä	Asp Leu Asp Thr Asn Ala Asp Lys Gln Leu Ser Phe Gl	Asp Lys Gln Leu Ser P	the Glu Glu Phe Ile		Pro Val Ala Gln Glu Asn Gln Gly Val Phe Phe Ser Gly Asp Ser	Phe Ser Gly Asp Ser Tyr
65	5 70	75	80		35 40	£ 5.
5 Me	Met Leu Met Ala Arg Leu Thr Trp Ala Ser His Glu Ly	Thr Trp Ala Ser His G	slu Lys Met His Glu	w	Leu Val Leu His Asn Gly Pro Glu Glu Val Ser His Leu His Leu Trp	Ser His Leu His Leu Trp
	8 8	06	95	•	. 55	09
ซี	Gly Asp Glu Gly Pro Gly His His Lys Pro Gly Leu Gly Glu Gly	His His His Lye Pro G	aly Leu Gly Glu Gly		Ile Gly Gln Gln Ser Ser Arg Asp Glu Gln Gly Ala Cys Ala Val Leu	31y Ala Cys Ala Val Leu
	100	105	110			. 80
Œ	Thr Pro				Ala Val His Leu Asn Thr Leu Leu Gly Glu Arg Pro Val Gln His Arg	Arg Pro Val Gln His Arg
01					. 85	56
					Glu Val Gln Gly Asn Glu Ser Asp Leu Phe Met Ser Tyr Phe Pro Arg	det Ser Tyr Phe Pro Arg
					100 105	110
Ÿ	<210> 50				Gly Leu Lys Tyr Gln Glu Gly Gly Val Glu Ser Ala Phe His Lys	Ser Ala Phe His Lys Thr
Ÿ	<211> 348				115 120	125
55	<212> PRT			. 18	Ser Thr Gly Ala Pro Ala Ala Ile Lys Lys Leu Tyr Gln Val Lys	beu Tyr Gln Val Lys Gly
∛	<213> Homo sapiens				130 135	140
₹	<220>.				Lys Lys Asn Ile Arg Ala Thr Glu Arg Ala Leu Asn Trp Asp Ser Phe	Jeu Asn Trp Asp Ser Phe
Ÿ	<221> Macrophage capping protein	g protein			145 150	155 160
Ÿ	<222> (1)(348)				Asn Thr Gly Asp Cys Phe ile Leu Asp Leu Gly Gln Asn Ile Phe Ala	3ly Gln Asn Ile Phe Ala
° .	<223> Accession No. as	Accession No. as of 10 Dec 2002; P40121	21		165 170	175
Ý	<400> 50			•	Trp Cys Gly Gly Lys Ser Asn Ile Leu Glu Arg Asn Lys Ala Arg Asp	Arg Asn Lys Ala Arg Asp
				•	. 180 185	190
ž	Met Tyr Thr Ala Ile Pro Gln Ser Gly Ser Pro Phe Pr	Gln Ser Gly Ser Pro P	Phe Pro Gly Ser Val		Leu Ala Leu Ala Ile Arg Asp Ser Glu Arg Gln Gly Lys Ala Gln Val	in Gly Lys Ala Gln Val
1	ın	10	15		195 . 200	205

Company Comp			
City Tie Val The Amp Gity Gity Gity Man For Gith Wel Lea Unit 213 220 220 Gity Pro Lyn Pro Ala Leu Lyn Gity Ann Pro Gity Gith Amp Leu Thir 223 2240 Ala Amp Lyn Ala Ann Ale Gin Ala Ala Ala Leu Tyr Lyn Val Ser Amp 255 Ala Thr Gity Gin Wet Ann Leu Chr Lyn Val Ala Amp Ser Ser Pro Phe 260 260 265 Ala Thr Gity Gin Wet Ann Leu Thr Lyn Val Ala Amp Ser Ser Pro Phe 260 260 265 Ala Thr Gity Leu Leu Lie Ser Amp Amp Cyn Phe Val Leu Map Ann Gity 275 Ala Thr Gity Leu Leu Lie Ser Amp Amp Cyn Phe Val Leu Map Ann Gity 275 Ala Thr Gity Leu Leu Lie Ser Amp Amp Cyn Phe Val Leu Map Ann Gity 275 Gith Any Ala Ala Leu Gin Val Ala Gity Arg Lyn Ala Ann Gity Arg Gity 230 Gith Any Ala Pro Ann Thr Gin Val Ala Gity Phe Lie Ser Arg Wet 310 Gith Any Ala Pro Ann Thr Gin Val Gity Hay Gity 313 Ser Pro Lie Phe Lyn Gin Phe Phe Lyn Gity Any Try Lyn 275 Ala 345 Ala Ala Ala Leu Gin Phe Phe Lyn Lyn 275 Ala 345 Ala Ala Ala Leu Gin Phe Phe Lyn Lyn 275 Ala Ala Ala Leu Gin Phe Phe Lyn Lyn 275 Ala Ala Ala Leu Gin Phe Phe Lyn Lyn 275 Ala Ala Ala Leu Chi Ala Ala Leu Chi Ala Ala Chi Ala Ala Chi Ala Ala Leu Chi Ala Ala Ala Ala Ala Chi Ala Ala Ala Ala Chi Ala	·	. 153/335	154/335
216 Fro Lygs Fro Ana Leau Lygs Gilu Gily Ann Pero Gilu Gilu Ango Leau Tint 225		Glu Ile Val Thr Asp Gly Glu Glu Pro Ala Glu Met Ile Gln Val Leu	<220>
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Ala Thr Gly Gln Met Aan Ala Gln Ala Ala Leu Tyr Lys Val Ser Asp 245 Ala Thr Gly Gln Met Aan Leu Thr Lys Val Ala Asp Ser Ser Pro Phe 260 265 270 Ala Leu Glu Leu Leu Ile Ser Amp Asp Gry Ser Nam Gly 275 280 280 280 280 280 280 280 380 Glu Arg Gln Ala Ala Gln Val Ala Glu Gly Pre Ile Ser Arg Met 305 310 315 326 Glu Arg Gln Ala Ala Leu Gln Val Glu He Lys Glu Gly Arg Lys Glu 326 337 340 345 250 338 346 250 270 338 330 337 346 250 270 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 381 380 380		Gly Pro Lys Pro Ala Leu Lys Glu Gly Asn Pro Glu Glu Asp Leu Thr	<222> (1). (346)
Ala Thr Gly Gln Met Ann Lau thr Lya Val Ber Ser Pro Phe 250 Ala Thr Gly Gln Met Ann Lau thr Lya Val Ala Arp Ser Ser Pro Phe 260 271 272 283 Ala Thr Gly Gln Met Ann Lau thr Lya Val Lau Arp Ser Ser Pro Phe 272 273 274 275 275 276 277 278 270 278 278 279 270 278 278 279 270 278 279 270 270 270 271 270 271 272 270 270		230 235	<223> Accession No. as of 10 Dec 2002: P04083
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260 265 270 215 280 285 10 275 280 285 10 10 Leu Leu Leu Leu Leu Hap Amp Cys Phe Val Leu Amp Am Gly 275 280 285 280 285 290 295 300 310 315 320 310 311 312 320 310 315 320 335 310 315 320 335 330 311 312 330 335 335 312 313 313 335 335 313 314 315 315 335 314 315 316 315 315 315 315 315 316 315 315 315 315 4212 807 807 807 807 807 807 807 807 807 4212 807 807 807 807 807 807 807 807 807 4212 807 807 807 807 807 807 807 807 4213 807 807 807 807 807 807 807 807 4213 807 807 807 807 807 807 807 807 4213 807 807 807 807 807 807 807 807 4213 807 807 807 807 807 807 807 807 807 4213 807 807 807 807 807 807 807 807 807 807 807 4213 807		Ala Thr Gly Gln Met Asn Leu Thr Lyg Val Ala Asp Ser Ser Pro Phe	Met Ala Met Val Ser Glu Phe Leu Lys Gln Ala Trp Phe Ile Glu Asn
Ala Leu Glu Leu Leu Ile Ser Amp Amp Cym Phe Val Leu Amp Amn Gly 230 230 230 240 250 250 250 250 250 250 25		265	5 10
10 10 10 10 10 10 10 10		Ala Leu Glu Leu Leu Ile Ser Asp Asp Cys Phe Val Leu Asp Asn Gly	Glu Glu Glu Tyr Val Gln Thr Val Lys Ser Ser Lys Gly Gly Fro
1996 299 295 300 Glu Arg Gln Ala Ala Leu Gln Val Ala Glu Gly Phe Ile Ser Arg Wet 305 310 315 320 Gln Tyr Ala Pro Asn Thr Gln Val Glu Ile Leu Pro Gln Gly Arg Glu 315 Ser Pro Ile Phe Lys Gln Phe Phe Lys Asp Trp Lys 340 345 4212> 51 4213> 346 4212> PRT 42113> 1000 saplens		275 280	20 25
Giu Arg Gin Ala Ala Leu Gin Val Ala Giu Giy Phe Ile Ser Arg Met 305 316 315 316 315 320 Gin Tyr Ala Pro Asn Thr Gin Val Giu Ile Leu Pro Gin Giy Arg Giu 325 330 335 Ser Pro Ile Phe Lys Gin Phe Phe Lys Asp Trp Lys 340 345 4211> 346 4211> PRT 42113> Homo sappiens		Leu Cys Gly Lys Ile Tyr Ile Trp Lys Gly Arg Lys Ale Asn Glu Lys	Gly Ser Ala Val Ser Pro Tyr Pro Thr Phe Asn Pro Ser Ser Asp Val
Glu Arg Gln Ala Ala Leu Gln Val Ala Glu Gly Phe Ile Ser Arg Met 305 310 315 320 Gln Tyr Ala Pro Asn Thr Gln Val Glu Ile Leu Pro Gln Gly Arg Glu 325 330 335 Ser Pro Ile Phe Lys Gln Phe Phe Lys Asp Trp Lys 340 345 4210> 51 4211> 346 4212> PRT 4213> Homo sapiens		. 295	40
315 310 315 320 315	•	Glu Arg Gln Ala Ala Leu Gln Val Ala Glu Gly Phe Ile Ser Arg Met	Ala Ala Leu His Lys Ala Ile Met Val Lys Gly Val Asp Glu Ala Thr
Gln Tyr Ala Pro Asn Thr Gln Val Glu Ile Leu Pro Gln Gly Arg Glu 325 330 335 Ser Pro Ile Phe Lys Gln Phe Phe Lys Asp Trp Lys 340 345 <210> 51 <211> 346 <212> PRT <2113 Homo sapiens		310 315	55
Ser Fro IIe Phe Lys Gln Phe Phe Lys Asp Trp Lys 340 345 <210> 51 <211> 346 <211> Homo sepiens 335 335 335 346 345 246 247 248 249 249 240 240 240 240 240 240			
Ser Pro Ile Phe Lys Gln Phe Phe Lys Asp Trp Lys 340 345 (210> 51 (211> 346 (212> PRT (213> Homo sapiens		. 330	70 75
346 345 20 20 210 211 211 212 212 213 Homo sapiens 223 Homo sapiens 224 225		Ser Pro 11e Phe Lys Gln Phe Phe Lys Asp Trp Lys	Lys Ala Ala Tyr Leu Gln Glu Thr Gly Lys Pro Leu Asp Glu Thr Leu
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Homo sepiens			120
Homo sapiens		<212> PRT	Gly Leu Gly Thr Asp Glu Asp Thr Leu Ile Glu Ile Leu Ala Ser Arg
			135

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		155	155/335				156/335		
	Thr Asn Lys Glu	Thr Asn Lys Glu Ile Arg Asp Ile Asn Arg Val Tyr Arg	n Arg Val Tyr	Arg Glu Glu Leu		Lys Ile Leu Va	Lys ile Leu Val Ala Leu Cys Gly Gly Asn	y Asn	
	145	150	155	160		340	345	ı,	
	Lys Arg Asp Leu	Lys Arg Asp Leu Ala Lys Asp Ile Thr Ser Asp Thr Ser	r Ser Asp Thr	Ser Gly Asp Phe					
		165	170	175					
	5 Arg Asn Ala Leu	Arg Asn Ala Leu Leu Ser Leu Ala Lys Gly Asp Arg Ser	s Gly Asp Arg	Ser Glu Asp Phe		5 <210> 52			
	180	185	ر م	190		<211> 469			
	Gly Val Asn Glu	Gly Val Asn Glu Asp Leu Ala Asp Ser Asp Ala Arg Ala	r Asp Ala Arg ?	Ala Leu Tyr Glu		<212> PRT			
	195	200	.,	205		<213> Homo sapiens			
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-	10 .210	215	220			10 <221> Keratin,	<221> Keratin, type II cytoskeletal	. 1.	
	Leu Thr Thr Arg	Leu Thr Thr Arg Ser Tyr Pro Gln Leu Arg Arg Val Phe	u Arg Arg Val E	Phe Gln Lys Tyr		<222> (1)(469)	(6		
	. 225	230	235	240		<223> Accessio	Accession No. as of 10 Dec 2002; P08729	002: P08729	
	Thr Lys Tyr Ser 1	Thr Lys Tyr Ser Lys His Asp Met Asn Lys Val Leu Asp	Lys Val Leu A	Asp Leu Glu Leu		<400> 52			
		245	250	255					
. 15		Lys Gly Asp Ile Glu Lys Cys Leu Thr Ala Ile Val Lys	: Ala Ile Val L	Lys Cys Ala Thr		15 Met Ser Ile His	Phe Ser Ser Pro Val	Met Ser 11e His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala	Ala Ala
	260	. 265	,0	270		, , ,	3	10	15
	Ser Lys Pro Ala I	Ser Lys Pro Ala Phe Phe Ala Glu Lys Leu His Gln Ala	Leu His Gln A	Ala Met Lys Gly		Phe Ser Gly Arg	Gly Ala Gln Val Arg	Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly	Pro Gly
	. 275	. 280	8	285	•	. 20	. 25	30	
	Val Gly Thr Arg !	Val Gly Thr Arg His Lys Ala Leu Ile Arg Ile Met Val	Arg Ile Met V	Al Ser Arg Ser		Gly Leu Gly Ser	Ser Ser Leu Tyr Gly	Gly Leu Gly Ser Ser Leu Tyr Gly Leu Gly Ale Ser Arg Pro Arg	Pro Arg
70	0 290	295	300		2	. 35	40	ij	
	Glu ile Asp Met A	Glu ile Asp Met Asn Asp ile Lys Ala Phe Tyr Gln Lys	Phe Tyr Gln L	ys Met Tyr Gly		Val Ala Val Arg	Ser Ala Tyr Gly Gly	Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg	ile Arg
	305	310	315	320		. 20	55	09	
	Ile Ser Leu Cys C	lle Ser Leu Cys Gln Ala Ile Leu Asp Glu Thr Lys Gly	Glu Thr Lys G	ily Asp Tyr Glu		Glu Val Thr Ile	Asn Gln Ser Leu Leu	Glu Val Thr Ile Asn Gln Ser Lou Leu Ala Pro Leu Arg Leu Asp Ala	isp Ala
	m	325	330	335		65	70	75	80

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Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Glu Ser Glu Gln 1	Gln Ile Lys	Lys Cys Ser Arg Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu	Gln Thr Lys Phe Glu
58		275 280	285
Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg E	Arg Phe Leu	Thr Leu Gln Ala Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr	Asp Leu Arg Asn Thr
100 105 .		290 295	300
5 Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu G	Leu Gln Glu	5 Arg Asn Glu Ile Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala	Gln Arg Leu Gln Ala
115 120 125		305 310 315	320
Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu A	Glu Ala Gln	Glu ile Asp Asn ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala ile	Leu Glu Ala Ala Ile
130 135 140		325 330	. 335
ile Ala Gly Leu Arg Gly Gin Leu Glu Ala Leu Gin Val Asp G	Asp Gly Gly	Ala Glu Ala Glu Glu Arg Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala	Lys Asp Ala Arg Ala
10 145 150 155	160	10 340 345	350
Arg Leu Glu Gln Gly Leu Arg Thr Met Gln Asp Val Val Glu A	Glu Asp Phe	Lys Gin Giu Leu Giu Ala Ala Leu Gin Arg Ala Lys Gin Asp Met	Ala Lys Gln Asp Met
165 170 1	175	. 355 360	365
Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala G	Ala Glu Asn	Ala Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala	Ser Val Lys Leu Ala
180 185 190		370 375	380
15 Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys		15 Leu Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu	Leu Glu Gly Glu Glu
. 195 200 205			400
Val Glu Leu Glu Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe	kan Phe	Ser Arg Leu Ala Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met	Asn Ile Ser Val Met
210 215 220		. 405 410	415
Leu Arg Thr Leu Asn Glu Thr Glu Leu Thr Glu Leu Gln Ser Gln Ile	in ile	. Asn Ser Thr Gly Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu	Ile Gly Leu Thr Leu
225 . 230 235	240	. 420 425	430
Ser Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser L	er Leu Asp	Gly Gly Thr Met Gly Ser Asn Ala Leu Ser Phe Ser Ser Ser Ala Gly	Ser Ser Ser Ala Gly
245 . 250 2:	255	435 440	445
Leu Asp Gly lle lle Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala	et Ala	Pro Gly Leu Leu Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg	Ala Ser Ala Ser Arg
. 260 265 270		450 455	460

••	WO 2004/055519 PCT/EP2003/014057 159/335 AZG Ser Ale Arg Asp	WO 2004/055519 160/335 160/335 PCT/EP2003/014057
	5 <210> 53 <211> 836 <212> PRT <213> Homo sapiens	5 Thr Gln Arg Tyr Ser Asp Ala Ser Lys Leu Arg Glu Glu Ile Glu Gly 115 120 125 Lys Gly Ser Phe Thr Tyr Phe Ala Pro Ser Asn Glu Ala Trp Asp Asn 130 135 140
9		Leu Asp Ser Asp lie Arg Gly Leu Glu Ser Asn Val Asn Val Glu 10 145 150 155 160 Leu Leu Asn Ala Leu His Ser His Met ile Asn Lys Arg, Met Leu Thr 165 170 175 Lys Asp Leu Lys Asn Gly Met Ile Ile Pro Ser Met Tyr Asn Asn Leu 180 185 190
S	1 15 10 Pro Phe Leu Pro Met Phe Ser Leu Leu Leu Leu Leu Leu lle Val 1 15 10 15 Asn Pro Ile Asn Ala Asn Asn His Tyr Asp Lys Ile Leu Ala His Ser 20 25 30 Arg Ile Arg Gly Arg Asp Gln Gly Pro Asn Val Cys Ala Leu Gln Gln	15 Gly Leu Phe Ile Asn His Tyr Pro Asn Gly Val Val Thr Val Asn Cys 195 200 205 Ale Arg Ile Ile His Gly Asn Gln Ile Ala Thr Asn Gly Val Val His 210 215 220 Val Ile Asp Arg Val Leu Thr Gln Ile Gly Thr Ser Ile Gln Asp Phe
20	135 40 45 11e Leu Gly Thr Lys Lys Lys Tyr Phe Ser Thr Cys Lys Asn Trp Tyr 50 55 60 1ys Lys Ser Ile Cys Gly Gln Lys Thr Thr Val Leu Tyr Glu Cys Cys	11e Glu Ala Glu Asp Asp Leu Ser Ser Phe Arg Ala Ala Ala Ile Thr 245 250 255 Ser Asp Ile Leu Glu Ala Leu Gly Arg Asp Gly His Phe Thr Leu Phe
	65 70 75 80	260 265 270

	WO 2004/055519 FCT/EP2003/014057	D57 WO 2004/055519 PCT/EP2003/0140	003/014
	Ala Pro Thr Asn Glu Ala Phe Glu Lys Leu Pro Arg Gly Val Leu Glu	Ala Val Cys Ile Glu Asn Ser Cys Met Glu Lys Gly Ser Lys Gln Gly	ιλ
	275 280 285	465 470 475 . 480	30
	Arg Phe Met Gly Asp Lys Val Ala Ser Glu Ala Leu Met Lys Tyr His	Arg Asn Gly Ala Ile His Ile Phe Arg Glu Ile Ile Lys Pro Ala Glu	กูเ
	290 295 300	485 490 495	
'n	i Ile Leu Asn Thr Leu Gln Cys Ser Glu Ser Ile Met Gly Gly Ala Val	5 Lyg Ser Leu His Glu Lys Leu Lys Gln Asp Lys Arg Phe Ser Thr Pho	91
	305 310 315 320	. 500 505 510	
	Phe Glu Thr Leu Glu Gly Asn Thr Ile Glu Ile Gly Cys Asp Gly Asp	Leu Ser Leu Glu Ala Ala Asp Leu Lys Glu Leu Thr Gln Pro	6
	325 330 335	515 520 525	
	Ser ile Thr Val Asn Gly Ile Lys Met Val Asn Lys Lys Asp ile Val	Gly Asp Trp Thr Leu Phe Val Pro Thr Asn Asp Ala Phe Lys Gly Met	Ť.
2	340 345 350	10 530 535 540	
	Thr Asn Asn Gly Val Ile His Leu Ile Asp Gln Val Leu Ile Pro Asp	Thr Ser Glu Glu Lys Glu Ile Leu Ile Arg Asp Lys Asn Ala Leu Gln	4
	355 360 . 365	545 550 555 560	. 05
	Ser Ala Lys Gln Val Ile Glu Leu Ala Gly Lys Gln Gln Thr Thr Phe	Asn Ile Ile Leu Tyr His Leu Thr Pro Gly Val Phe Ile Gly Lys Gly	٠ <u>٠</u>
	370 375 380	565 570 . 575	•
15	Thr Asp Leu Val Ala Gln Leu Gly Leu Ala Ser Ala Leu Arg Pro Asp	15 Phe Glu Pro Gly Val Thr Asn Ile Leu Lys Thr Thr Gln Gly Ser Lys	
	385 390 395 400	065 585 085	
	Gly Glu Tyr Thr Leu Leu Ala Pro Val Asn Asn Ala Phe Ser Asp Asp	Ile Phe Leu Lys Glu Val Asn Asp Thr Leu Leu Val Asn Glu Leu Lys	В.
	405 410 415	595 600	
	Thr Leu Ser Met Val Gln Arg Leu Leu Lys Leu Ile Leu Gln Asn His	Ser Lys Glu Ser Asp Ile Met Thr Thr Asn Gly Val Ile His Val Val	٠ ټ
20	420 425 430	20 610 615 620	
	Ile Leu Lys Val Lys Val Gly Leu Asn Glu Leu Tyr Asn Gly Gln Ile	Asp Lys Leu Tyr Pro Ala Asp Thr Pro Val Gly Asn Asp Gln Leu	ne ne
	435 440 445	625 630 635 640	
	Leu Glu Thr Ile Gly Gly Lys Gln Leu Arg Val Phe Val Tyr Arg Thr	Leu Glu Ile Leu Asn Lys Leu Ile Lys Tyr Ile Gln Ile Lys Phe Val	귾
	450 455 460	645 . 650 . 655	

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	WO 2004/055519		PCT/EP2003/014057	WO 2004/055519 PCT	PCT/R.P2003/
		163/335		. 164/33\$	
	Arg Gly Ser Thr Phe Lys Glu ile Pro Val Thr Val Tyr Thr Thr Lys	le Pro Val Thr Val Tyr Thr T			
	999	665 670			
	lle ile Thr Lys Val Val Glu Pro Lys ile Lys Val ile Glu Gly Ser	o Lys Ile Lys Val Ile Glu G	ly Ser	<210> 54	
	675 68	680 685		<211> 687	•
'n	Leu Gin Pro ile ile Lys Thr Glu Gly Pro Thr Leu Thr Lys Val Lys	u Gly Pro Thr Leu Thr Lys V.		5. <212> PRT	
	690 695	700		<213> Homo sapiens	
	Ile Glu Gly Glu Pro Glu Phe Arg Leu Ile Lys Glu Gly Glu Thr Ile	g beu Ile bys Glu Gly Glu T	hr ile	<220>	
	705 710	715	720	<221> Protein-glutamine gamma-glutamyltransferase	•.
	Thr Glu Val Ile His Gly Glu Pro Ile Ile Lys Lys Tyr Thr Lys Ile	o ile ile Lys Lys Tyr Thr L	ya ile	<222> (1)(687)	
01	725	730 73	735 10	<223> Accession No. P21980	*
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	740	745 750			
	Arg lle ile Thr Gly Pro Glu ile Lys Tyr Thr Arg ile Ser Thr Gly	e Lys Tyr Thr Arg Ile Ser Th	nr Gly	Met Ala Glu Glu Leu Val Leu Glu Arg Cys Asp Leu Glu Leu Glu Thr	1 Thr
	755 760	0 765		1 5 10 15	
15	Gly Gly Glu Thr Glu Glu Thr Leu Lys Lys Leu Leu Glu Glu Glu Val	1 Lys Lys Leu Leu Gln Glu Gl	lu Val	Asn Gly Arg Asp His His Thr Ala Asp Leu Cys Arg Glu Lys Leu Val	ı Val
	775	780		20 25 30	
	Thr Lys Val Thr Lys Phe Ile Glu Gly Gly Asp Gly His Leu Phe Glu	ı Gly Gly Asp Gly His Leu Ph		Val Arg Arg Gly Gln Pro Phe Trp Leu Thr Leu His Phe Glu Gly Arg	. Arg
	785 . 790	795	800	35 40 45	
	Asp Glu Glu Ile Lys Arg Leu Gen Gly Asp Thr Pro Val Arg Lys	ı Gln Gly Asp Thr Pro Val Ar	ву пув	Asin Tyr Glu Ala Ser Val Asp Ser Leu Thr Phe Ser Val Val Thr	c Gly
70	808	810 815	.5		
	Leu Gin Ale Asn Lys Lys Val Gin Gly Ser Arg Arg Arg Leu Arg Glu	ı Gly Ser Arg Arg Arg Leu Ar	9 Glu	Pro Ala Pro Ser Gln Glu Ala Gly Thr Lys Ala Arg Phe Pro Leu Arg	1 Arg
	820	825 830		65 70 75	90
	Gly Arg Ser Gln			Asp Ala Val Glu Gly Asp Try Thr Ala Thr Val Val Asp Gln Gln	dln d
	. 835			56 . 06 . 58	

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Asp Cys Thr Leu Ser Leu Gln Leu Thr Thr Pro Ala Asn Ala Pro Ile	Arg Cys Leu Gly Ile Pro Thr Arg Vel Val Thr Asn Tyr Asn Ser Ala
100 105 110	290 295 300
Gly Leu Tyr Arg Leu Ser Leu Glu Ala Ser Thr Gly Tyr Gln Gly Ser	His Asp Gln Asn Ser Asn Leu Leu Ile Glu Tyr Phe Arg Asn Glu Phe
115 120 125	305 310 315 320
5 Ser Phe Val Leu Gly His Phe Ile Leu Leu Phe Asn Ala Trp Cys Pro	Gly Glu Ile Gln Gly Asp Lys Ser Glu Met Ile Trp Asn Phe His Cys
. 130 135 140	325 330 335
Ala Asp Ala Val Tyr Leu Asp Ser Glu Glu Glu Arg Gln Glu Tyr Val	Trp Val Glu Ser Trp Met Thr Arg Pro Asp Leu Gln Pro Gly Tyr Glu
145 .150 .155 .160	340 345 350
Leu Thr Gin Gin Gly Phe Ile Tyr Gin Gly Ser Ala Lys Phe Ile Lys	Gly Trp Gln Ala Leu Asp Pro Thr Pro Gln Glu Lys Ser Glu Gly Thr
10 165 170 175	355 360 365
Asn Ile Pro Trp Asn Phe Gly Gln Phe Glu Asp Gly Ile Leu Asp Ile	Tyr Cys Cys Gly Pro Val Pro Val Arg Ala Ile Lys Glu Gly Asp Leu
180 185 190	370 375 380
Cys Leu Ile Leu Leu Asp Val Asn Pro Lys Phe Leu Lys Asn Ala Gly	Ser Thr Lys Tyr Asp Ala Pro Phe Val Phe Ala Glu Val Asn Ala Asp
	385 390 395 400
15 Arg Asp Cys Ser Arg Ser Ser Pro Val Tyr Val Gly Arg Val Val	Val Val Asp Trp Ile Gin Gin Asp Asp Gly Ser Val His Lys Ser Ile
210 215 220 ·	405 . 410 415
Ser Gly Met Val Asn Cys Asn Asp Asp Gln Gly Val Leu Leu Gly Arg	Asn Arg Ser Leu Ile Val Gly Leu Lys Ile Ser Thr Lys Ser Val Gly
225 230 235 240	420 425 430
Trp Asp Asn Asn Tyr Gly Asp Gly Val Ser Pro Met Ser Trp Ile Gly	Arg Asp Glu Arg Glu Asp Ile Thr His Thr Tyr Lys Tyr Pro Glu Gly
20 245 256 255 20	435 440 . 445
Ser Val Asp Ile Leu Arg Arg Trp Lys Asn His Gly Cys Gln Arg Val	Ser Ser Glu Glu Arg Glu Ale Phe Thr Arg Ala Asn His Leu Asn Lys
260 265 270	450 455 460
Lys Tyr Gly Gln Cys Trp Val Phe Ala Ala Val Ala Cys Thr Val Leu	Leu Ala Glu Lys Glu Glu Thr Gly Met Ala Met Arg Ile Arg Val Gly
275 280 285	465 470 475 480

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Gln Ser Met Asn Met Gly Ser Asp Phe Asp Val Phe Ala	al Phe Ala His Ile Thr	Leu Lys Ala Val Lys Gly Phe Arg Asn Val 11e Ile Gly Pro Ala
485 490	495	675 680 685
Asn Asn Thr Ala Glu Glu Tyr Val Cys Arg Leu Leu Leu	eu Leu Leu Cys Ala Arg	
500 505	510	
5 Thr Val Ser Tyr Asn Gly Ile Leu Gly Pro Glu Cys Gly	Thr Lys Tyr	5 <210> 55
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Leu Leu Asn Leu Asn Leu Glu Pro Phe Ser Glu Lys Ser	lu Lys Ser Val Pro Leu	<212> PRT
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Cys ile Leu Tyr Glu Lys Tyr Arg Asp Cys Leu Thr Glu	eu Thr Glu Ser Asn Leu	<220>
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565 570	575	<223> Accession No. as of 10 Dec 2002: P52565
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580 585	065	
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. 009 565	605	1 5 10 15
Leu Gln Asn Pro Leu Pro Val Ala Leu Glu Gly Cys Thr	y Cys Thr Phe Thr Val	Glu Asn Glu Glu Asp Glu His Ser Val Asn Tyr Lys Pro Pro Ala Gln
610 615	620	. 20 25 30
Glu Gly Ala Gly Leu Thr Glu Glu Gln Lys Thr Val Glu	r Val Glu Ile Pro Asp	Lys Ser Ile Gln Glu Ile Gln Glu Leu Asp Lys Asp Asp Glu Ser Leu
20 625 630 635	5 . 640 20	
Pro Val Glu Ala Gly Glu Glu Val Lys Val Arg Met Asp Leu Leu Pro	g Met Asp Leu Leu Pro	Arg Lys Tyr Lys Glu Ala Leu Leu Gly Arg Val Ala Val Ser Ala Asp
. 645 650		. 09
Leu His Met Gly Leu His Lys Leu Val Val Asn Phe Glu Ser Asp Lys	n Phe Glu Ser Asp Lys	Pro Asn Val Pro Asn Val Val Thr Gly Leu Thr Leu Val Cys Ser
660 665	670	65 70 75 80

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169/335		170/335	
Ser Ala Pro Gly Pro Leu Glu Leu Asp Leu Thr Gly Asp Leu Glu Ser	eu Glu Ser	<222> (1)(492)	
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Phe Lys Lys Gin Ser Phe Val Leu Lys Glu Gly Val Glu Tyr Arg Ile	Yr Arg 11e	<400> 56 .	
100 105 11	110		
5 Lys.Ile Ser Phe Arg Val Asn Arg Glu Ile Val Ser Gly Met Lys	Tyr	5 Met Pro Thr Asn Gly Leu His Gln Val Leu Lys Ile Gln Phe Gly Leu	the Gly Leu
115 120 125		1 5 10	15
ile Gin His Thr Tyr Arg Lys Gly Val Lys ile Asp Lys Thr Asp Tyr	hr Asp Tyr	Val Asn Asp Thr Asp Arg Tyr Leu Thr Ala Glu Ser Phe.Gly Phe Lys	ily Phe Lys
130 135 140		20 25 3	30
Met Val Gly Ser Tyr Gly Pro Arg Ala Glu Glu Tyr Glu Phe Leu Thr	he beu Thr	Val Asn Ala Ser Ala Pro Ser Leu Lys Arg Lys Gln Thr Trp Val Leu	TP Val Leu
10 145 150 155	160 10	35 40 45	· ·
Pro Val Glu Glu Ala Pro Lys Gly Met Leu Ala Arg Gly Ser Tyr	er fyr Ser	Glu Pro Asp Pro Gly Gln Gly Thr Ala Val Leu Leu Arg Ser Ser His	er Ser His
165		90 22 60	
Ile Lys Ser Arg Phe Thr Asp Asp Lys Thr Asp His Leu Ser	eu Ser Trp	Leu Gly Arg Tyr Leu Ser Ala Glu Glu Asp Gly Arg Val Ala Cys Glu	la Cys Glu
180 185 190	•	65 70 75	80
15 Glu Trp Asn Leu Thr Ile Lys Lys Asp Trp Lys Asp	51	Ala Glu Gln Pro Gly Arg Asp Cys Arg Phe Leu Val Leu Pro Gln Pro	ro Gln Pro
. 200		98	95
		Asp Gly Arg Trp Val Leu Arg Ser Glu Pro His Gly Arg Phe Phe Gly	ne Phe Gly
•	,	100 105 1.	110
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20 <211> 492	20	115 120. 125	
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<220>		Ser Val Ser Arg Arg Tyr Val His Leu Cys Pro Arg Glu Asp Glu	u Asp Glu
<221> Fascin 2		145 150 155	160

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Met Ala Ala Asp Gly Asp Lys Pro Trp Gly Val Asp Ala Leu Leu Thr	Val Cys Met Lys Lys Asn Gly Gln Leu Ala Ala Ile Ser Asp Phe Val
165 170 175	355 096 355
Leu 11e Phe Arg Ser Arg Arg Tyr Cys Leu Lys Ser Cys Asp Ser Arg	Gly Lys Asp Glu Glu Phe Thr Leu Lys Leu Ile Asn Arg Pro Ile Leu
180 185 190	370 375 380
5 Tyr Leu Arg Ser Asp Gly Arg Leu Val Trp Glu Pro Glu Pro Arg Ala	5 Val Leu Arg Gly Leu Asp Gly Phe Val Cys His His Arg Gly Ser Asn
. 195 200 205	385 390 395 400
Cys Tyr Thr Leu Glu Phe Lys Ala Gly Lys Leu Ala Phe Lys Asp Cys	Gln Leu Asp Thr Asn Arg Ser Val Tyr Asp Val Phe His Leu Ser Phe
210 215 220	405 . 410 415
Amp Gly His Tyr Leu Ala Pro Val Gly Pro Ala Gly Thr Leu Lys Ala	Ser Asp Gly Ala Tyr Arg Ile Arg Gly Arg Asp Gly Gly Phe Trp Tyr
10 225 230 235 240	10 420 425 430
Gly Arg Asn Thr Arg Pro Gly Lys Asp Glu Leu Phe Asp Leu Glu Glu	Thr Gly Ser His Gly Ser Val Cys Ser Asp Gly Glu Arg Ala Glu Asp
245 250 . 255	435 440 445
Ser His Pro Gln Val Val Leu Val Ala Ala Asn His Arg Tyr Val Ser	Phe Val Phe Glu Phe Arg Glu Arg Gly Arg Leu Ala 11e Arg Ala Arg
260. 265 . 270	450 . 455 460
15 Val Arg Gln Gly Val Asn Val Ser Ala Asn Gln Asp Asp Glu Leu Asp	15 Ser Gly Lys Tyr Leu Arg Gly Gly Ala Ser Gly Leu Leu Arg Ala Asp
	465 470 475 480
His Glu Thr Phe Leu Met Gln Ile Asp Gln Glu Thr Lys Lys Cys Thr	Ala Asp Ala. Pro Ala Gly Thr Ala Leu Trp Glu Tyr
290 295 300	485 490
Phe Tyr Ser Thr Gly Gly Tyr Trp Thr Leu Val Thr His Gly Gly	
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Ile His Ala Thr Ala Thr Gln Val Ser Ala Asn Thr Met Phe Glu Met	<210> 57
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Glu Trp Arg Gly Arg Arg Val Ala Leu Lys Ala Ser Asn Gly Arg Tyr	<212> PRT
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1433 1434	PCLIEF2003/01405/ 173/335 rin (Actin-depolymerizing factor) (ADF)	PARAINEMAGRITA
4221> Descrin (Actin-dapolymeriting factor) (ADP) 4222> (1)(168) 4222> (1)(168) 4222> (1)(168) 4222> (1)(168) 4222> (1)(168) 4222> (1)(168) 4223> (1)(168) 4225 (1)(168) 4225 (1)(168) 425 (1)(168) 426 (1)	Destrin (Actin-depolymerizing factor) (ADF)	174/335
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4223- Accession No. as of 29 August 2003; F19282 4400- 57 Net Ala Ser City Val Cin Val Ala Asp Ciu Val Cys Arg Ile Phe Tyr 1		lu Gly Cys Pro Val
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App Met Lys val Arg Lys Cys Ser Thr Pro Glu Glu Ile Lys Lys Arg 20 23 30 10 1ys Lys Ala Val Ile Phe Cys Leu Ser Ala Asp Lys Lys Cys Ile Ile 35 40 45 45 45 46 45 46 45 46 47 48 48 40 48 48 40 48 40 48 40 48 40 48 40 48 40 48 40 48 40 48 40 40		
Amp Met Lys Val Arg Lys Cys Ser The Fro Glu Glu Lie Lys Lys Arg 20 135 40 40 40 40 40 40 40 40 40 4	5 10 15	
156 Lys Ala Val Ite Phe Cye Leu Ser Ala Asp Lys Lys Cye Ite Ite 35 40 45 45 45 45 46 45 47 48 48 48 48 48 48 48 48 48		112> PRT
1.55 Lys Ala Val lie Phe Cys Leu Ser Ala Asp Lys Cys Ile lie 35 40 45 45 Val Glu Glu Glu Gly Lys Glu Ile Leu Val Gly Asp Val Gly Val Thr Ile 50 55 60 60 70 75 80 Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 85 90 95 Glu Glu Leu Met Phe Leu Trp Ala Pro Glu Leu Pro Leu Lys Phe 110 110 20 20 315 Glu Gly Ile Lys His Glu Cys Gln Ala Asm Gly Pro Glu Asp Leu Asn 115 116 117 118 119	20 25 30 10	113> Homo sapiens
135 40 45 45 46 45 47 48 48 48 48 48 48 48		750>
50 55 60 Thr Asp Pro Phe Lys His Phe Val Gly Met Leu Pro Glu Lys Asp Cys 15 65 70 75 80 Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 95 95 Glu Glu Leu Met Phe Phe Leu Trp Ala Pro Glu Leu Lys 110 20 Ser Lys Met Lle Tyr Ala Ser Ser Lys Asp Ala Lle Lys Lys Phe 125 120 Glu Gly Leu Wet Lie Tyr Ala Ser Ser Lys Asp Ala Lle Lys Lys Phe 125 126 Glu Gly Leu Wet Lie Tyr Ala Ser Ser Lys Asp Ala Lle Lys Lys Phe 125 126 Glu Gly Lie Lys His Glu Cys Gln Ala Asm Gly Pro Glu Asp Leu Asm 130 135	40 45	
The Asp Pro Phe Lys His Phe Val Gly Met Leu Pro Glu Lys Asp Cys 65 Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 85 Glu Glu Leu Met Phe Phe Lau Try Ala Pro Glu Leu Ala Pro Leu Lys 100 20 Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 116 117 118 118 119 119 119 119 110 110		
The Asp Pro Phe Lys His Phe Val Gly Met Leu Pro Glu Lys Asp Cys 65 Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 85 90 95 Glu Glu Leu Met Phe Phe Leu Trp Ala Pro Glu Leu Ala Pro Leu Lys 100 100 105 Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 120 125 Glu Gly Ile Lys His Glu Cys Gln Ala Asn Gly Pro Glu Asp Leu Asn 130 140 140	09 55	
Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 85 Glu Glu Leu Met Phe Phe Leu Trp Ala Pro Glu Leu Ala Pro Leu Lys 100 100 105 Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 Gln Gly Ile Lys His Glu Cys Gln Ala Asn Gly Pro Glu Asp Leu Asn 130 135 Arg Tyr Ala Ser Phe Glu Thr Lys Glu Asp Leu Asn 140 20	Thr Asp Pro Phe Lys His Phe Val Gly Met Leu Pro Glu Lys Asp Cys	00> 58
Arg Tyr Ala Leu Tyr Asp Ala Ser Phe Glu Thr Lys Glu Ser Arg Lys 85 Glu Glu Leu Met Phe Phe Leu Trp Ala Pro Glu Leu Ala Pro Leu Lys 100 100 100 100 100 115 115 120 125 Glu Glu Leu Asp Pro Leu Lys Phe 115 120 125 Glu Glu Leu Asp Pro Glu Leu Asp Pro Leu Lys Phe 115 120 125 Glu Glu Lys Phe 130 135 140	70 75	
Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys		Thr Ala Asn Gly Thr Ala Glu Ala Val Gln Ile Gln Phe Gly Leu Ile
Glu Glu Leu Met Phe Leu Trp Ala Pro Glu Leu Ala Pro Leu Lys 100 100 105 110 Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 120 125 Gln Gly Ile Lys His Glu Cys Gln Ala Asn Gly Pro Glu Asp Leu Asn 130 130 140	56 . 06	5 10
Ser Lys Met Ile Tyr Ala Ser Ser Lys Asp Ala Ile Lys Lys Phe 115 126 Gln Gly Ile Lys His Glu Cys Gln Ala Asn Gly Pro Glu Asp Leu Asn 130 135 20 20 21 25 21 25 21 26 27 28 29 20 20 20 20 20 20 20 20 20 20 20 20 20		Asn Cys Gly Asn Lys Tyr Leu Thr Ale Glu Ala Phe Gly Phe Lys Val
		25
		Asn Ala Ser Ala Ser Ser Leu Lys Lys Lys Gln Ile Trp Thr Leu Glu
	. 120 . 125	. 40
135 140		n Pro Pro Asp Glu Ala Gly Ser Ala Ala Val Cys Leu Arg Ser His
	135 140	50 55 60

WO 2004/055519 175/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057 176/335
Leu Gly Arg Tyr Leu Ale Ale Asp Lys Asp Gly Asn Val	y Asn Val Thr Cys Glu	Gln Ser Cys Ala Gln Val Val Leu Gln Ala Ala Asn Glu Arg Asn val
65 70 75	80	260 265 270
Arg Glu Val Pro Gly Pro Asp Cys Arg Phe Leu Ile Val	u lle Val Ala His Asp	Ala Asn Gln Asp
85 90	95	275 280 285
5 Asp Gly Arg Trp Ser Leu Gln Ser Glu Ala His Arg Arg	3 Arg Arg Tyr Phe Gly	5 Asp Gln Glu Thr Phe Gln Leu Glu Ile Asp Arg Asp Thr Lys Lys Cye
100 105	110	290 295 300
Gly Thr Glu Asp Arg Leu Ser Cys Phe Ala Gln Thr Val	Thr Val Ser Pro Ala	Ala Phe Arg Thr His Thr Gly Lys Tyr Trp Thr Leu Thr Ala Thr Gly
115 . 120	125	305 310 315 320
Glu Lys Trp Ser Val His Ile Ala Met His Pro Gln Val	Gln Val Asn Ile Tyr	Gly Val Gln Ser Thr Ala Ser Ser Lys Asn Ala Ser Cys Tyr Phe Asp
10 130 135	140	325 330 335
Ser Val Thr Arg Lys Arg Tyr Ala His Leu Ser Ala Arg	Ala Arg Pro Ala Asp	Ile Glu Trp Arg Arg Arg Ile Thr Leu Arg Ala Ser Asn Gly Lys
145 150 155	160	340 345 350
Glu Ile Ala Val Asp Arg Asp Val Pro Trp Gly Val Asp Ser Leu Ile	Val Asp Ser Leu Ile	Phe Val Thr Ser Lys Lys Asn Gly Gln Leu Ala Ala Ser Val Glu Thr
165 170	175	355 360 365
15 Thr Leu Ala Phe Gin Asp Gin Arg Tyr Ser Val Gin Thr Ala Asp His	Gln Thr Ala Asp His.	is Ala Gly Asp Ser Glu Leu Phe Leu Met Lys Leu Ile Asn Arg Pro Ile
180 · 185	. 190	376 376 380
Arg Phe Leu Arg His Asp Gly Arg Leu Val Ala Arg Pro Glu Pro Ala	Arg Pro Glu Pro Ala	. Ile Val Phe Arg Gly Glu His Gly Phe Ile Gly Cys Arg Lys Val Thr
195 200	205	385 390 395 400
Thr Gly Tyr Thr Leu Glu Phe Arg Ser Gly Lys Val Ala Phe Arg Asp	Val Ala Phe Arg Asp	Gly Thr Leu Asp Ala Asn Arg Ser Ser Tyr Asp Val. Phe Gln Leu Glu
20 210 215	. 220	20 405 410 415
Cys Glu Gly Arg Tyr Leu Ala Pro Ser Gly Pro Ser Gly Thr Leu Lys	Ser Gly Thr Leu Lys	Phe Asn Asp Gly Ala Tyr Asn Ile Lys Asp Ser Thr Gly Lys Tyr Trp
225 230 235	240	420 425 430
Ala Gly Lys Ala Thr Lys Val Gly Lys Asp Glu Leu Phe Ala Leu Glu	Leu Phe Ala Leu Glu	Thr Val Gly Ser Asp Ser Ala Val Thr Ser Ser Gly Asp Thr Pro Val
245 . 250 .	255	435 440 445

WO 2004/055519	PCT/EP2003/014057	WO 2004/055519 PCT/RP	PCT/EP2003/01
Asp Phe Phe Glu Phe Cys Asp Tyr Asn Lys Val Ala Ile Lys Val		Gly Arg Phe frp Asp Tyr Leu Arg frp Val Gln Thr Leu Ser Glu Gln	Gln
450 455 . 460		50 55 60	
Gly Gly Arg Tyr Leu Lys Gly Asp His Ala Gly Val Leu Lys Ala Ser	s Ala Ser	Val Gln Glu Glu Leu Leu Ser Ser Gln Val Thr Gln Glu Leu Arg Ale	Ala
465 470 475	. 480	65 . 70 75	90
5 Ala Glu Thr Val Asp Pro Ala Ser Leu Trp Glu Tyr		Leu Met Asp Glu Thr Met Lys Glu Leu Lys Ala Tyr Lys Ser Glu Leu	Leu
485		85 . 90 85 E	
		Glu Glu Gln Leu Thr. Pro Val Ala Glu Glu Thr Arg Ala Arg Leu Ser	Ser
	٠.	100 105 . 110	
<210> 59		Lys Glu Leu Gln Ala Ala Gln Ala Arg Leu Gly Ala Asp Met Glu Asp	Asp
0 <211> 317	10	115 120 . 125	
<212> PRT		Val Cys Gly Arg Leu Val Gln Tyr Arg Gly Glu Val Gln Ala Met Leu	Leu
<213> Homo sapiens		130 135 140	
<220>		Gly Gln Ser Thr Glu Glu Leu Arg Vel Arg Leu Ale Ser His Leu Arg	Arg
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5 <222> (1)(317)		Lys Leu Arg Lys Arg Leu Leu Arg Asp Ala Asp Asp Leu Gln Lys Arg	Arg
<223> Accession No. as of 29 August 2003: P02649		165 170 175	
<400> 59		Leu Ala Val Tyr Gln Ala Gly Ala Arg Glu Gly Ala Glu Arg Gly Leu	ren
		180 185 190	
Met Lys Val Leu Trp Ala Ala Leu Leu Val Thr Phe Leu Ala Gly Cys	Gly Cys	Ser Ala Ile Arg Glu Arg Leu Gly Pro Leu Val Glu Gln Gly Arg Val	Val
1 5 10	15	195 , 200 205	
Gin Ala Lys Val Glu Gin Ala Val Glu Thr Glu Pro Glu Pro	Glu Pro Glu Leu	Arg Ala Ala Thr Val Gly Ser Leu Ala Gly Gln Pro Leu Gln Glu Arg	er.
20 25 30		210 215 220	
Arg Gln Gln Thr Glu Trp Gln Ser Gly Gln Arg Trp Glu Leu	Glu Leu Ala Leu	Ala Gin Ala Trp Gly Glu Arg Leu Arg Ala Arg Met Glu Glu Met Gly	31y
35 40 45		225 230 235 24	240

20

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WO 2004/05551	179/335	PCT/EP2003/014057	WO 2004/055519 180/335	PCT/EP2003/014057
Ser Arg Tl	Ser Arg The Arg Asp Arg Leu Asp Glu Val Lys Glu Gln V	Val Ala Glu	Gly Thr Val Thr Val Arg Tyr Ala Pro Ser Glu Ala Gly Leu His Glu	ily Leu His Glu
	245 250	255	. 20 . 25	30
Val Arg Al	Val Arg Ala Lys Leu Glu Glu Gln Ala Gln Gln Ile Arg L	reu Gln Ala	Met Asp Ile Arg Tyr Asp Asn Met His Ile Pro Gly Ser Pro Leu Gln	er Pro Leu Gln
	260 . 265 . 2	270	35 40 . 41	45.
5 Glu Ala Phe	Gln Ala Arg Leu Lys Ser Trp Phe Glu Pro	Leu Val Glu	5 Phe Tyr Val Asp Tyr Val Asn Cys Gly His Val Thr Ala Tyr Gly Pro	la Tyr Gly Pro
275	5 280 . 285		09 SS 05	
Asp Met Gl	Asp Met Gln Arg Gln Trr Ala Gly Leu Val Glu Lys Val Gln Ala Ala	n Ala Ala	Gly Leu Thr His Gly Val Val Asn Lys Pro Ala Thr Phe Thr Val Asn	he Thr Val Asn
290	295 300		75 70 75	. 08
Val Gly Th	Val Gly Thm Ser Ala Ala Pro Val Pro Ser Asp Asn His		Thr Lys Asp Ala Gly Gly Gly Leu Ser Leu Ala Ile Glu Gly Pro	le Glu Gly Pro
10 305	310 315	1	10 85 90	95
			Ser Lys Ala Glu Ile Ser Cys Thr Asp Asn Gln Asp Gly Thr Cys	ly Thr Cys Ser
			100 105	110
<210> 60			Val Ser Tyr Leu Pro Val Leu Pro Gly Asp Tyr Ser Ile Leu Val Lys	le Leu Val Lys
<211> 838			115 120 125	25
15 <212> PRT		=	is Tyr Asn Glu Gln His Val Pro Gly Ser Pro Phe Thr Ala Arg Val Thr	la Arg Val Thr
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<221> hypo	hypothetical 88.6 kDa protein		145 150 155	160
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			180 185	190
Met Pro Ser	Met Pro Ser Gly Lys Val Ala Gin Pro Thr Ile Thr Asp Asn Lys Asp	Lys Asp	Leu Arg Aen Gly His Vel Gly Ile Ser Phe Val Pro Lys Glu Thr Gly	s Glu Thr Gly
H	. 10 .	15	195 200 205	ı,
				-

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	WO 2004/055519		PCT/EP2003/014057	3/014057	WO 2004/055519			PCT/EP2003/0
		181/333				182/335		
	Glu His Leu Val His V.	Glu His Leu Val His Val Lys Lys Asn Gly Gln His Val Ala Ser	is Val Ala Ser Ser	:	His Thr Val Ser	His Thr Val Ser Val Lys Tyr Lys Gly Gln His Val Pro Gly Ser Pro	lln His Vel Pro Gly :	Ser Pro
	210	215 22	220			405 . 4.	410	415
	Pro lle Pro Val Val I	Pro ile Pro Vel Val Ile Ser Gln Ser Glu Ile Gly Asp Ale Ser Arg	ly Asp Ala Ser Arg		Phe Gln Phe Thr	Phe Gin Phe Thr Val Gly Pro Leu Gly Glu Gly Gly Ala His Lys Val	ilu Gly Gly Ala His I	ys Val
	225 , 23	230 235	240		420	425	430	
ıv		Val Arg Val Ser Gly Gln Gly Leu His Glu Gly His Thr Phe Glu Pro	is Thr Phe Glu Pro	5	5 Arg Ala Gly Gly	Arg Ala Gly Gly Pro Gly Leu Glu Arg Ala Glu Ala Gly Val Pro Ala	la Glu Ala Gly Val E	ro Ala
	245	250	255		435	440	445	
	Ala Glu Phe Ile Ile A	Ala Glu Phe Ile Ile Asp Thr Arg Asp Ala Gly Tyr Gly Gly Leu Ser	yr Gly Gly Leu Ser		Glu Phe Ser Ile	Glu Phe Ser Ile Trp Thr Arg Glu Ala Gly Ala Gly Gly Leu Ala Ile	ly Ala Gly Gly Leu A	la Ile
	. 260	265	270		450	455	460	
	Leu Ser Ile Glu Gly Pa	Leu Ser 11e Glu Gly Pro Ser Lys Val Asp Ile Asn Thr Glu Asp Leu	sn Thr Glu Asp Leu		Ala Val Glu Gly	Ala Val Glu Gly Pro Ser Lys Ala Glu Ile Ser Phe Glu Asp Arg Lys	le Ser Phe Glu Asp A	rg Lys
2	275	280	285	10		470	475	480
	Glu Asp Gly Thr Cys At	Glu Asp Gly Thr Cys Arg Val Thr Tyr Cys Pro Thr Glu Pro Gly Asn	hr Glu Pro Gly Asn		Asp Gly Ser Cys (Asp Gly Ser Cys Gly Val Ala Tyr Val Val Gln Glu Pro Gly Asp Tyr	al Gln Glu Pro Gly A	sp Tyr
	290	295 300			•	485 49	490 4	495
•	Tyr ile ile Asn ile $\mathbf{b}_{\mathbf{j}}$	Tyr ile ile Aen ile Lys Phe Ala Asp Gin His Val Pro	al Pro Gly Ser Pro		Glu Val Ser Val I	Glu Val Ser Val Lys Phe Asn Glu Glu His Ile Pro Asp Ser Pro Phe	is Ile Pro Asp Ser P	ro Phe
	305 31	310 315	320		200	505	510	
15	•	Phe Ser Val Lys Val Thr Gly Glu Gly Arg Val Lys Glu	rs Glu Ser Ile Thr	S1		Val Val Pro Val Ala Ser Pro Ser Gly Asp Ala Arg Arg Leu Thr Val	sp Ala Arg Arg Leu T	hr Val
	325	330	335		515	520	. 525	
	Arg Arg Arg Arg Ala Pi	Arg Arg Arg Arg Ala Pro Ser Val Ala Asn Val Gly Ser His Cys Asp	ly Ser His Cys Asp		Ser Ser Leu Gln (Ser Ser Leu Gln Glu Ser Gly Leu Lys Val Asn Gln Pro Ala Ser Phe	al Asn Gln Pro Ala S	er Phe
	340	345	350		530	535	540	
	Leu Ser Leu Lys Ile Pr	Leu Ser Leu Lys Ile Pro Glu Ile Ser Ile Gln Asp Met Thr Ala Gln	sp Met Thr Ala Gln		Ala Val Ser Leu A	Ala Val Ser Leu Asn Gly Ala Lys Gly Ala Ile Asp Ala Lys Val His	la Ile Asp Ala Lys Va	al His
70	355	360	365		545	550	555	260
	Val Thr Ser Pro Ser Gl	Val Thr Ser Pro Ser Gly Lys Thr His Glu Ala Glu Ile Val Glu Gly	lu Ile Val Glu Gly		Ser Pro Ser Gly A	Ser Pro Ser Gly Ala Leu Glu Glu Cys Tyr Val Thr Glu Ile Asp Gln	T Val Thr Glu Ile A	ap Gln
	370	375 380	06		ن	565 570		575
	Glu Asn His Thr Tyr Cy	Glu Asn His Thr Tyr Cys Ile Arg Phe Val Pro Ala Glu Met Gly Thr	la Glu Met Gly Thr		Asp Lys Tyr Ala V	Asp Lys Tyr Ala Val Arg Phe Ile Pro Arg Glu Asn Gly Val Tyr Leu	g Glu Asn Gly Val Ty	r Leu
	385 390	395	400		. 280	r cc r	c c	

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119 AND VAI LYA Phe Am Gity The His II e Pero Gity Sear Pro Phe Lya 615 600 605 605 605 605 605 605 605 605 60		183/335	184/335	٠
115 ANY VAI GIV GIA PPO GIA HA GIA GIA AND PPO GIA LON VAI Serr 610 611 612 613 623 624 Ala Tyr Giy Ala Giy Lou Giu Giy Giy Vai The Giy Ann PPO Ala Giu 625 626 627 628 629 Phe Vai Vai Ann The Ser Ann Ala Giy Ala Giy Ala Lou Ser Vai The 646 650 650 650 651 650 651 650 651 650 651 650 651 650 652 110 650 651 650 651 650 651 650 651 650 651 650 651 652 650 653 650 651 652 650 651 650 651 650 651 650 651 650 651 650 651 650 652 653 650 653 650 650 650 650 650		Ile Asp Val Lys Phe Asn Gly Thr His Ile Pro Gly Ser Pro Phe Lys	Val His Gly Pro Arg Thr Pro Cys Glu Glu Ile Leu Val Lys His Val	
119 Arg val City Clu City Clu City Clu Wile City Val Thr City Ann Pro City Leau Val City City Ann City City City City City City City City		009	790 795	
Signature Sign		Ile Arg Val Gly Glu Pro Gly His Gly Gly Asp Pro Gly Leu Val Ser	Gly Ser Arg Leu Tyr Ser Val Ser Tyr Leu Leu Lys Asp Lys Gly Glu	
Ala Tyr City Ala City Lea Cit City City Val Thr City Ann Pro Ala City Eds		615	810	
645 640 Phe Val Val Ann Thi Ser Ann Ala Gly Ala Leu Ser Val Thir 645 650 650 650 650 650 650 670 Gly Tyr Arg Val Thi Tyr Thi Pro Met Ala Pro Gly Ser Tyr Leu Lie 610 Gly Tyr Arg Val Thi Tyr Thi Pro Met Ala Pro Gly Ser Tyr Leu Lie 610 610 610 610 610 610 610 61				
Phe Val Val Ann Thr Ser Ann Ale Gly Ala Leu Ser Val Thr 645 650 656 670 Gly Pyr Arg Val Thr Tyr Thr Pro Mot Ala Pro Gly Ser Tyr Leu Lie 675 680 685 Ser Ile Lya Tyr Cly Cly Cly Fro Tyr Ha Ile Cly Gly Ser Tyr Leu Lie 675 680 685 887 100 Ala Lya Val Thr Cly Pro Arg Leu Val Ser Ann Ha Ser Leu Hia Glu 720 Thr Ser Ser Val Thr Oly Pro Arg Leu Thr Lya Ala Thr Cys Ala Pro 725 720 725 740 745 745 750 760 770 770 770 770 770 77		630 635	825	
660 665 670 Clu Cys Pro Glu 660 665 670 670 670 671 677 Azg Val Thr Tyr Thr Pro Hot Ala Pro Gly Ser Tyr Lau Ile 673 680 685 Ser Ile Lys Tyr Gly Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys 690 695 Ala Lys Val Thr Gly Pro Arg Leu Val Ser Am His Ser Leu His Glu 705 Thr Ser Ser Val Phe Val App Ser Leu Thr Cys Ala Pro 725 Glu His Gly Ala Pro Gly Pro Gly Pro Ala And Ala Ser Lys Val Tys 740 Ala Lys Gly Leu Gly Pro Gly Pro Ala And Ala Ser Lys Val Cly Wal Cly Wal Cly Wal Cly Ala Pro 745 Ala Lys Gly Leu Gly Pro Gly Pro Ala And Ala Ser Lys Val Cly Gly Cly Pro Ala And Ala Ser Lys Wal Cly Wal Cly Leu Ser Lys Ala Tyr Val Gly Glu Cly Ser Ser Ser 755 760 Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Val Gly Glu Lys Ser Ser 755 760 Ala Lys Gly Leu Gly Leu Ser Lys Ala Cly And And Het Leu Leu Val Gly 770 770 770 770		Phe Val Val Asn Thr Ser Asn Ala Gly Ala Gly Ala Leu Ser Val Thr	Tyr Arg Val Val Pro	
11e Aap Gily Pro Ser Lyse Val Lyse Met Anap Cys Gin Glu Cys Pro Glu		650	835	
619, Tyr Arg Val Thr Tyr Thr Pro Not Ala Pro Gly Ser Tyr Leu Ile 675 680 685 680 685 88r Ile Lys Tyr Gly Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys 690 Ala Lys Val Thr Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys 690 Ala Lys Val Thr Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys 705 Thr Ser Ser Val Phe Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro 725 730 730 730 740 740 745 750 Ala Lys Gly Leu Gly Pro Gly Pro Ala Asp Ala Ser Lys Val Val 740 740 745 750 760 765 770 770 770 770 77		Ile Asp Gly Pro Ser Lys Val Lys Met Asp Cys Gln Glu Cys Pro Glu		
61y fyr Arg Val Thr fyr Thr Pro Met Ala Fro Gly Ser fyr Leu Ile 675 680 685 680 685 680 Ala Lys Tyr Gly Gly Pro fyr His Ile Gly Gly Ser Pro Phe Lys 699 710 715 710 715 710 715 720 716 717 718 719 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 715 710 710		599 . 099	01	
Ser Ile Lys Tyr Gly Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys 630 Ala Lys Val Thr Gly Pro Arg Leu Val Ser Ann His Ser Leu His Glu 705 Thr Ser Ser Val Phe Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro 725 730 730 730 730 740 740 745 750 Ala Lys Val Val 740 745 750 Ala Lys Gly Pro Gly Pro Ala Asp Ala Ser Lyg Val Val 740 745 750 760 Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Val Gly Gln Lys Ser Ser 755 Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Asn Het Leu Leu Val Gly 770 771 772 773 780		Gly Tyr Arg Val Thr Tyr Thr Pro Met Ala Pro Gly Ser Tyr Leu Ile		
Ser lie Lys Tyr Gly Gly Pro Tyr His lie Gly Gly Ser Pro Phe Lys 690 Ala Lys Val Thr Gly Pro Arg Leu Val Ser Asm His Ser Leu His Glu 705 710 715 710 715 720 716 717 720 718 719 719 719 719 719 719 710 715 710 715 710 715 720 735 Gln His Gly Ala Pro Gly Pro Ala Asp Ala Ser Leu His Glu 746 746 746 746 746 750 760 760 776 780 770 770 770 77		675 680		
Ala Lys Val Thr Gly Pro Arg Leu Val Ser Asn His Ser Leu His Glu 705 Thr Ser Ser Val Phe Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro 716 717 718 719 719 719 719 719 719		Ser ile Lys Tyr Gly Gly Pro Tyr His Ile Gly Gly Ser Pro Phe Lys	<212> PRT	
105 710 715 720 720 720 720 720 720 720 720 720 720 720 720 720 720 725 720 725 720 725 725 720 725 720 725 720 725 720 725 720 725 720 725 720		695		
715 716 7170 715 720 Thr Ser Ser Val Phe Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro 725 730 735 Gln His Gly Ala Pro Gly Pro Gly Pro Ala Asp Ala Ser Lys Val Val 740 745 750 Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Val Gly Gln Lys Ser Ser 755 760 765 Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Met Leu Leu Val Gly 770 775 780		15. Ala Lys Val Thr Gly Pro Arg Leu Val Ser Asn His Ser Leu His Glu		
Thr Ser Ser Val Phe Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro 725 Gln His Gly Ala Pro Gly Pro Ala Asp Ala Ser Lys Val Val 740 745 750 Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Val Gly Gln Lys Ser Ser 755 760 765 Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Met Leu Leu Val Gly 770 770		710 715	<221> human alpha enolase	
Gin His Gly Ala Pro Gly Pro Ala Asp Ala Ser Lys Val Val 740 745 750 Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Val Gly Gln Lys Ser Ser 755 760 765 Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Met Leu Leu Val Gly 770 775 786		Thr Ser Ser Val Phe Val Asp Ser Leu Thr Lys Ala Thr Cys Ala Pro	<222> (1)(433)	
Gln His Gly Ala Pro Gly Pro Ala Asp Ala Ser Lys Val Val 740 Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Val Gly Gln Lys Ser Ser 755 760 765 Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Met Leu Leu Val Gly 770 770 770		730	<223>. Accession No. as of 29 August 2003; P06733	•
Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Vel Gly Gln Lys Ser Ser 755 760 765 Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Met Leu Leu Val Gly 770 770 770 780		Gln His Gly Ala Pro Gly Pro Gly Pro Ala Asp Ala Ser Lys Val	<400> 61	
		740 745	. 20	
		Ala Lys Gly Leu Gly Leu Ser Lys Ala Tyr Val Gly Gln Lys Ser Ser	Ser Ile Leu Lys Ile His Ala Arg Glu Ile Phe Asp Ser Arg Gly Asn	
		. 760	10	
775 780 25	•	Phe Thr Val Asp Cys Ser Lys Ala Gly Asn Asn Met Leu Leu Val Gly	Pro Thr Val Glu Val Asp Leu Phe Thr Ser Lys Gly Leu Phe Arg Ala	
		. 775	. 25	

	WO 2004/055519 185/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057	
	Ala Val Pro Ser Gly Ala Ser Thr Gly Ile Tyr Glu Ala Leu	Ala Leu Glu Leu	Leu Leu Lys Thr Ala Ile Gly Lys Ala Gly Tyr Thr Asp Lys Val Val	
	35 40		225 230 235 240	
	Arg Asp Asn Asp Lys Thr Arg Tyr Met Gly Lys Gly Val Ser	Val Ser Lys Ala	ile Gly Met Asp Val Ala Ala Ser Glu Phe Phe Arg Ser Gly Lys Tyr	
	09 25 05		245 . 250 . 255	
5	Val Glu His Ile Asn Lys Thr Ile Ala Pro Ala Leu Val	. Val Ser Lys Lys	Asp Leu Asp Phe Lys Ser Pro Asp Asp Pro Ser Arg Tyr Ile Ser Pro	
	65 70 75	. 08	260 265 270	
	Leu Asn Val Thr Glu Gln Glu Lys Ile Asp Lys Leu Met Ile	Met Ile Glu Met	Asp Gln Leu Ala Asp Leu Tyr Lys Ser Phe Ile Lys Asp Tyr Pro Val	
	85		275 280 285	
	Asp Gly Thr Glu Asn Lys Ser Lys Phe Gly Ala Asn Ala Ile	Ala Ile Leu Gly	Val Ser Ile Glu Asp Pro Phe Asp Gln Asp Asp Trp Gly Ala Trp Gln	
10	100 . 105	110	290 295 300	
	Val Ser Leu Ala Val Cys Lys Ala Gly Ala Val Glu Lys Gly	Lys Gly Val Pro	Lys Phe Thr Ala Ser Ala Gly Ile Gln Val Val Gly Asp Asp Leu Thr	
	115 120	125	305 310 315 320	
	Leu Tyr Arg His Ile Ala Asp Leu Ala Gly Asn Ser Glu Val	Glu Val Ile Leu	Val Thr Asn Pro Lys Arg Ile Ala Lys Ala Val Asn Glu Lys Ser Cys	
	130 135 140		325 330 335	
15	Pro Val Pro Ala Phe Asn Val Ile Asn Gly Gly Ser His Ala	His Ala Gly Asn	Asn Cys Leu Leu Leu Lys Val Asn Gln Ile Gly Ser Val Thr Glu Ser	
	. 145 . 150 . 155	160	340. 345 350	
	Lys Leu Ala Met Gln Glu Phe Met Ile Leu Pro Val Gly Ala	Gly Ala Ala Asn	Leu Gln Ala Cys Lys Leu Ala Gln Ala Asn Gly Trp Gly Val Met Val	
	165 170	175	355 360 365	
	Phe Arg Glu Ala Met Arg Ile Gly Ala Glu Val Tyr His Asn	. His Asn Leu Lys	Ser His Arg Ser Gly Glu Thr Glu Asp Thr Phe Ile Ala Asp Leu Val	
2	180 185	. 20	370 375 380	
	Asn Val Ile Lys Glu Lys Tyr Gly Lys Asp Ala Thr Asn Val	: Asn Val Gly Asp	Val Gly Leu Cys Thr Gly Gln Ile Lys Thr Gly Ala Pro Cys Arg Ser	
	195 200	205	385 390 400	
	Glu Gly Gly Phe Ala Pro Asn Ile Leu Glu Asn Lys Glu Gly	Glu Gly Leu Glu	Glu Arg Leu Ala Lys Tyr Asn Gln Leu Leu Arg Ile Glu Glu Glu Leu	
	210 215 220		405 410 415	

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Gly Ser Lys Ala Lys Phe Ala Gly Arg Asn Phe Arg Asn	Ala Gly Arg Asn Phe Arg A	sn Pro Leu Ala		Gly Asn Pro Ala Pro Thr Ser Asn His Gly Pro Asp Ala Thr Glu Ala	p Ala Thr Glu Ala
420	425	430		55 70 75	08
Lys				Glu Glu Asp Phe Val Asp Pro Trp Thr Val Gln Thr Ser Ser Ala Lys	r Ser Ser Ala Lys
·.				06	. 56
W.			in '	Gly ile Asp Tyr Asp Lys Leu ile Val Arg Phe Gly Ser Ser Lys ile	Y Ser Ser Lys Ile
				100 105	
<210> 62				Asp Lys Glu Leu ile Asn Arg ile Glu Arg Ala Thr Gly Gln Arg Pro	r Gly Gln Arg Pro
<211> 471				115 . 120	125
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10 <213> Homo sapiens			10	130 . 135 140.	
<220>				Gln Val Leu Asp Ala Tyr Glu Asn Lys Lys Pro Phe Tyr Leu Tyr Thr	Tyr Leu Tyr Thr
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<222> (1)(471)				Gly Arg Gly Pro Ser Ser Glu Ala Met His Vel Gly His Leu Ile Pro	His Leu Ile Pro
<223> Accession No. as o	Accession No. as of 29 August 2003; P23381			165 170	175
15 <400> 62			15	Phe Ile Phe Thr Lys Trg Leu Gln Asp Val Phe Asn Val Pro Leu Val	val Pro Leu Val
				180 . 185	190
Met Pro Asn Ser Glu Pro Ala Ser Leu Leu Glu Leu Phe	ala Ser Leu Leu Glu Leu P	he Asn Ser Ile		ile Gin Met Thr Asp Asp Glu Lys Tyr Leu Trp Lys Asp Leu Thr Leu	Asp Leu Thr Leu
1 5	10	15	•.	195 200	205
Ala Thr Gln Gly Glu Leu Val Arg Ser Leu Lys Ala Gly	al Arg Ser Leu Lys Ala G	ly Asn Ala Ser	æ	Asp Gin Ala Tyr Ser Tyr Ala Val Glu Asn Ala Lys Asp 11e 11e Ala	Asp Ile Ile Ala
20 20	25	30	20	210 215 220	
Lys Asp Glu Ile Asp Ser Ala Val Lys Met Leu Val Ser	ala Val Lys Met Leu Val S	er Leu Lys Met		Cys Gly Phe Asp Ile Asn Lys Thr Phe Ile Phe Ser Asp Leu Asp Tyr	Asp Leu Asp Tyr
35	40 45	ın	N	225 230 235	240
Ser Tyr Lys Ala Ala Ala Gly Glu Asp Tyr Lys Ala Asp	ily Glu Asp Tyr Lys Ala A	sp Cys Pro Pro	Σ	Met Gly Met Ser Ser Gly Phe Tyr Lys Asn Val Val Lys Ile Gln Lys	Lys 11e Gln Lys
50 . 5	. 09 92			245	255

WO 2004/055519 ·	189/335	PCT/EP2003/014057	WO 2004/055519 190/335	PCT/EP2003/014057
His Val Thr Phe Asn Gln Val Lys Gly Ile Phe Gly Phe		Thr Asp Ser	Arg Lys Glu Val Thr Asp Glu Ile Val Lys Glu Phe Met Thr Pro Arg	r Pro Arg
. 260	265	270	450 455 460	
Asp Cys Ile Gly Lys Ile Ser Phe Pro Ala Ile Gln Ala		Ala Pro Ser	Lys Leu Ser Phe Asp Phe Gln	
275 28	280 285		465 470	
5 Phe Ser Asn Ser Phe Pro Gln Ile Phe Arg Asp Arg Thr		Asp Ile Gin		
290 295	300			
Cys Leu Ile Pro Cys Ala Ile Asp Gln Asp Pro Tyr Phe		Arg Met Thr	· <210> 63	
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Glu Glu His Arg Gln Phe Gly Gly Asn Cys Asp Val Asp		Val Ser Phe	Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln	ogn Glu
385 390	395	. 007	1 5 10	15
Met Tyr Leu Thr Phe Phe Leu Glu Asp Asp Lys Leu		Glu GlnːIle	Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr	1 Phe Tyr
20 405	410	415	20 20 25 30	
Arg Lys Asp Tyr Thr Ser Gly Ala Met Leu Thr Gly Glu		Leu Lys Lys	Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser	ı Gln Ser
. 420	425	430	35 40 45	
Ala Leu Ile Glu Val Leu Gln Pro Leu Ile Ala Glu His		Gln Ala Arg	Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr	ser Thr
435 44	440 445		50 55 . 60	

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Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp		Tyr Glu Lys	Ala Gly Leu Leu Fhe Val Gly Gly Gly Ile Gly Gly Thr Ile Leu Tyr	Ile Leu Tyz
65 70	75	. 08	09 . \$5 . 05	
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu		Ser Ser Pro	Ala Lys Trp Asp Ser His Phe Arg Glu Ser Val Glu Lys Thr Ile Pro	Thr Ile Pro
85	06	95	. 65 70 75	08
5 Val Thr Lys Ser Phe Asn Arg Gly Glu Cys	ly Glu Cys		5 Tyr Ser Asp Lys Leu Phe Glu Met Val Leu Gly Pro Ala Ala Tyr Asn	Ala Tyr Asn
100	105			. 56
			Val Pro Leu Pro Lys Lys Ser Ile Gln Ser Gly Pro Leu Lys Ile	Lys Ile Ser
			100	110
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15 <222> (1)(758)	•		is Pro Ala Val Gln Pro Glu Glu Ser Leu Lys Thr Asp His Pro Glu Ile	Pro Glu Ile
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			180 185	190
Met Leu Arg Ala Cys Gln Leu Ser Gly Val Thr Ala Ala		Ala Gin Ser	Ser ile Arg Glu Arg Pro Pro Glu Glu Val Ala Ala Arg Leu Ala Gln	Leu Ala Gln
20 1 5	10	15	20 195 200. 205	
Cys Leu Cys Gly Lys Phe Val Leu Arg Pro Leu Arg Pro		Cys Arg Arg	Gln Glu Lys Gln Glu Gln Val Lys Ile Glu Ser Leu Ala Lys Ser Leu	Lys Ser Leu
20	25	30	210 . 215 . 220	
Tyr Ser Thr Ser Gly Ser Ser Gly Leu Thr Thr Gly Lys		Ile Ala Gly	Glu Asp Ala Leu Arg Gln Thr Ala Ser Val Thr Leu Gln Ala Ile Ala	Ala Ile Ala
35 .	455		225 230 235	240

77 WO 2004/055519 PCT/EP2003/014057	Ala Leu Glu Lys Gln Lys Leu Glu Glu Lys Arg Ala Phe Asp Ser Ala	435 440 445	Val Ala Lys Ala Leu Glu His His Arg Ser Glu Ile Gln Ala Glu Gln	. 450 455 460	5 Asp Arg Lye Ile Glu Glu Val Arg Asp Ala Met Glu Asn Glu Met Arg	465 470 475 480	Thr Gln Leu Arg Arg Gln Ala Ala Ala His Thr Asp His Leu Arg Asp	485 490 495	Val Leu Arg Val Gin Giu Giu Leu Lys Ser Giu Phe Giu Gin Asn	. 10 500 505 510	Leu Ser Glu Lys Leu Ser Glu Gln Glu Leu Gln Phe Arg Arg Leu Ser	515 520 525	Gin Giu Gin Val Asp Asn Phe Thr Leu Asp Ile Asn Thr Ala Tyr Ala	530 535 540	15 Arg Leu Arg Gly Ile Glu Gln Ala Val Gln Ser His Ala Val Ala Glu	. 545 550 555 560	Glu Glu Ala Arg Lys Ala His Gln Leu Trp Leu Ser Val Glu Ala Leu	565 570 575	Lys Tyr Ser Met Lys Thr Ser Ser Ala Glu Thr Pro Thr Ile Pro Leu	20 580 585 590	Gly Ser Ala Val Glu Ala Ile Lys Ala Asn Cys Ser Asp Asn Glu Phe	. 009 505
/01405						٠																
PCT/EP2003/014057	la His Ser Asn Ile Leu	255	ly Glu Lys Lys Ser Ala	270	lu Arg Arg Lys Ala Val	285	s Glu Glu Leu Glu Lys	300 .	s Glu Val Ala Gly Ala	320	eu His Asn Met Ile Val	. 335	la Ala Gin Ser Giu Ala	350	al Gln Ala Arg Asp Asp	365	lu Val Leu Pro Gly Trp	380	ys Leu Ser Thr Asp Asp	95 400	rg Ile Asp Gln Leu Asn	
PCT/EP2003/01405	Ala Gln Asn Ala Ala Val Gln Ala Val Asn Ala His Ser Asn Ile Leu	250 255	Lys Ala Ala Met Asp Asn Ser Glu Ile Ala Gly Glu Lys Lys Ser Ala	265 270	Gin Trp Arg Thr Val Glu Gly Ala Leu Lys Glu Arg Arg Lys Ala Val	280 285	Asp Glu Ala Ala Asp Ala Leu Leu Lys Ala Lys Glu Glu Leu Glu Lys	300 300	Met Lys Ser Val Ile Glu Asn Ala Lys Lys Lys Glu Val Ala Gly Ala	310 315 320	Lys Pro His Ile Thr Ala Ala Glu Gly Lys Leu His Asn Met Ile Val	330 . 335	Asp Leu Asp Asn Val Val Iys Iys Val Gln Ala Ala Gln Ser Glu Ala	345	Lys Val Val Ser Gin Tyr His Glu Leu Val Val Gin Ala Arg Asp Asp	360 365	Phe Lys Arg Glu Leu Asp Ser Ile Thr Pro Glu Val Leu Pro Gly Trp	375 380	Lys Gly Met Ser Val Ser Asp Leu Ala Asp Lys Leu Ser Thr Asp Asp	390 395 400	Leu Agn Ser Leu Ile Ala His Ala His Arg Arg Ile Asp Gln Leu Asn	

WO 2004/055519 PCT/EP2003/014057	5/014057 WO 2004/055519 196/335	PCT/EP2003/014057
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625 . 630 635 . 640	<221> Ribisome-binding protein 1	
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675 680 685	1 5 10	. 15
Lys Leu Leu Ser Tyr Ala Ser Tyr Cys Ile Glu His Gly Asp Leu Glu	Phe Met Val Val Ser Ala Ile Gly Ile Phe Leu Val Ser Thr Phe Ser	Thr Phe Ser
10 690 . 695 . 700	10 20 25 .3	.30
Leu Ala Ala Lys Phe-Val Asn Gln Leu Lys Gly Glu Ser Arg Arg Val	Met Lys Glu Thr Ser Tyr Glu Glu Ala Leu Ala Asn Gln Arg Lys Glu	Arg Lys Glu
705 . 710 715 720	35 40 45	
Ala Gin Asp Trp Leu Lys Giu Ala Ary Met Thr Leu Glu Thr Lys Gin	Met Ala Lys Thr His His Gln Lys Val Glu Lys Lys Lys Lys Glu Lys	Lys Glu Lys
725 730 735	09 25 09	
15 Ile Val Glu ile Leu Thr Ala Tyr Ala Ser Ala Val Gly Ile Gly Thr	15 Thr Val Glu Lys Lys Gly Lys Thr Lys Lys Lys Glu Glu Lys Pro Asn	Lys Pro Asn
740 745 750	65 70 75	08
Thr Gln Val Gln Pro Glu	Gly Lys Ile Pro Asp His Asp Pro Ala Pro Asn Val Thr Val Leu Leu	Val Leu Leu
755	90	. 36
	Arg Glu Pro Val Arg Ala Pro Ala Val Ala Val Ala Pro Thr Pro Val	Thr Pro Val
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<213> Homo saptens	130 135 140	

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		197/335		PC1/EP2003/014057			WO 2004/055519	198/335		PCT/EP2003/014
	Lys Val Ala L	Lys Val Ala Lys Val Glu Pro Ala Val Ser Ser Val Val Asn Ser Ile	Ser Ser Val Val	Asn Ser Ile		•	Asn Gin Gly Lys Lys Ale Glu Gly Ale Gin Asn Gin Gly Lys Lys Ale	Ala Glu Gly Ala Gl	in Asn Gln Gly Ly	Lys Ala
	145	150	155	160			340	345	350	
	Gln Val Leu T	Gln Val Leu Thr Ser Lys Ala Ala Ile Leu Glu Thr Ala Pro Lys Glu	Leu Glu Thr Ala	Pro Lys Glu			Glu Gly Ala Gln Asn Gln Gly Lys Lys Ale Glu Gly Ale Gln Asn Gln	Gln Gly Lys Lys Al	a Glu Gly Ala Gl	1 Asn Gln
		165	170	175			355	360	365	
Ŋ		Val Pro Met Val Val Val Pro Pro Val Gly Ala Lys Gly Asn Thr Pro	Gly Ala Lys Gly	Asn Thr Pro		ĸ	Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ser Glu Gly	Gly Ala Gln Asn Gl	n Gly Lys Lys Se	: Glu Gly
		180 185		190		•	370	375	380	
	Ala Thr Gly T	Ala Thr Gly Thr Thr Gln Gly Lys Lys Ala Glu Gly Thr Gln Asn Gln	Ala Glu Gly Thr	Gln Asn Gln			Ala Gln Aen Gln Gly Lys Lys Vel Glu Gly Ala Gln Asn Gln Gly Lys	Lys Lys Val Glu Gl	y Ala Gln Asn Gl	Gly LyB
	195	200	205			•	385	390	395	400
	Ser Lys Lys A	Ser Lys Lys Ala Glu Gly Ala Pro Asn Gln Gly Arg Lys Ala Glu Gly	Gln Gly Arg Lys	Ala Glu Gly			Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln	Gln Asn Gln Gly Ly	s Lys Ala Glu Gl	Ala Gln
10	210	215	220			01	. 405	410	0	415
	Thr Pro Asn G	Thr Pro Asn Gln Gly Lys Lys Thr Glu Gly Thr Pro Asn Gln Gly Lys	Gly Thr Pro Asn	Gln Gly Lys		•	Asn Gin Gly Lys Lys Ala Glu Gly Ala Gin Asn Gin Gly Lys Lys Ala	Ala Glu Gly Ala Gl	n Asn Gln Gly Ly	Lys Ala
	225	230	235	240			420	425	430	
	Lys Ala Glu G	Lys Ala Glu Gly Thr Pro Asn Gln Gly Lys Lys Ala	Lys Lys Ala Glu	Glu Gly Thr Pro	•		Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln	Gln Gly Lys Lys Al	a Glu Gly Ala Glı	Asn Gln
		245	250	255	. .		435	440	445	
15	Asn Gln Gly L	Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Val	Gln Asn Gln Gly	Lys Lys Val		51	Gly Lys Lys Ale Glu Gly Ale Gln Asn Gln Gly Lys Lys Ale Glu Gly	Gly Ala Gln Asn Gl	n Gly Lys Lys Ala	Glu Gly
	Ŕ	260 265		270			450	455	460	
	Asp Thr Thr P.	Asp Thr Thr Pro Asn Gln Gly Lys Lys Val Glu Gly Ala Pro Thr Gln	Val Glu Gly Ala	Pro Thr Gln			Ala Gln Asn Gin Gly Lys Lys Val Glu Gly Ala Gln Asn Gln Gly Lys	Lye Lys Val Glu Gl	y Ala Gln Asn Glr	Gly Lys
	. 275	280	285			•	. 465	470	475	480
	Gly Arg Lys A.	Gly Arg Lys Ala Glu Gly Ala Gln Asn Gln Ala Lys Lys Val Glu Gly	Gin Ala Lys Lys	val Glu Gly	•		Lys Ala Glu Gly Ala Gln Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln	Gln Asn Gln Gly Ly	B Lys Ala Glu Gly	Ala Gln
20	290	295	300			20	485	490		495
	Ala Gln Asn G	Ala Gln Aen Gln Gly Lys Lys Ala Glu Gly Ala Gln Aen Gln Gly Lye	Gly Ala Gln Asn	Gln Gly Lys			Asn Gln Gly Lys Lys Ala Glu Gly Ala Gln Asn Gln Gly Gln Lys Gly	Ala Glu Gly Ala Glı	n Asn Gln Gly Glr	гув С1у
	305	310	315	. 320			005	. 505	510	
	Lys Gly Glu G	Lys Gly Glu Gly Ala Gln Asn Gln Gly Lys Lys Al	Œ	Glu Gly Ala Gln			Glu Gly Ala Gln Asn Gln Gly Lys Lys Thr Glu Gly Ale Gln Gly Lys	Gln Gly Lys Lys Th	r Glu Gly Ala Glr	Gly Lys
		325	330	.335		•	515	520	. 222	

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_	WO 2004/055519		PCT/EP2003/014057	· WO 2004/055519	PCT/EP2003/014057
		199/335		. 200/335	
	Lys Ala Glu Arg Sea	Lys Ala Glu Arg Ser Pro Asn Gln Gly Lys Lys Gly Glu Gly Ala	u Gly Ala Pro	Ser Lys Leu Arg Glu Leu Asn Lys Glu Met Ala Ala Glu Lys Ala Lys	la Ala Glu Lys Ala Lys
	530	535 540		725 . 730	735
	ile Gln Gly Lys Lya	Ile Gin Gly Lys Lys Ala Asp Ser Val Ala Asn Gin Gly T	y Thr Lys Val	Ala Ala Ala Gly Glu Ala Lys Val Lys Lys Gln Leu Val Ala Arg Glu	in beu Val Ala Arg Glu
	545	550 555	. 095	740 745	750
'n	Glu Gly Ile Thr Asr	Glu Gly ile Thr Asn Gln Gly Lys Lys Ala Glu Gly Ser P	r Pro Ser Glu	5 Gin Glu rie Thr Ala Val Gin Ala Arg Met Gin Ala Ser Tyr Arg Glu	In Ala Ser Tyr Arg Glu
	. 565	5 570	575	755 760	765
	Gly Lys Lys Ala Gly	Gly Lys Lys Ala Glu Gly Ser Pro Asn Gln Gly Lys Lys Ala Asp Ala	s Ala Asp Ala	His Val Lys Glu Val Gln Gln Leu Gln Gly Lys Ile Arg Thr Leu Gln	/8 Ile Arg Thr Leu Gln
	280	585	069	277 077	. 084
	Ala Ala Asn Gln Gly	Ala Ala Asn Gln Gly Lys Lys Thr Glu Ser Ala Ser Val Gln Gly Arg	l Gln Gly Arg	Glu Gln Leu Glu Asn Gly Pro Asn Thr Gln Leu Ala Arg Leu Gln Gln	su Ala Arg Leu Gln Gln
9	595	600 605	:	10 785 . 790 . 75	800
	Asn Thr Asp Val Ale	Asn Thr Asp Val Ala Gln Ser Pro Glu Ala Pro Lys Gln Glu Ala Pro	n Glu Ala Pro	Glu Asn Ser Ile Leu Arg Asp Ala Leu Asn Gln Ala Thr Ser Gln Val	n Ale Thr Ser Gln Val
	610	615 620		805 810	. 815
	Ala Lys Lys Ser	Ala Lys Lys Lys Ser Gly Ser Lys Lys Lys Gly Glu Pro Gly Pro Pro	o Gly Pro Pro	Glu Ser Lys Cln Asn Ala Glu Leu Ala Lys Leu Arg Gln Glu Leu Ser	e Arg Gln Glu Leu Ser
	625	630 635	640	820 825	830
15	Asp Ala Asp Gly Pro	Asp Ala Asp Gly Pro Leu Tyr Leu Pro Tyr Lys Thr Leu V	al Ser Thr	15 Lys Val Ser Lys Glu Leu Val Glu Lys Ser Glu Ala Val Arg Gln Asp	u Ala Val Arg Gln Asp
	. 645	650		835 840	845
	Val Gly Ser Met Val	Val Gly Ser Met Val Phe Asn Glu Gly Glu Ala Gln Arg Leu Ile Glu	g Leu Ile Glu	Glu Gln Gln Arg Lys Ala Leu Glu Ala Lys Ala Ala Ala Phe Glu Lys	a Ala Ala Phe Glu Lys
	099	665		850 855	860
	ile beu Ser Glu bys	Ile Leu Ser Glu Lys Ala Gly Ile Ile Gln Asp Thr Trp His Lys	p His Lys Ala	Gin Val Leu Gin Leu Gin Ala Ser His Arg Glu Ser Glu Glu Ala Leu	u Ser Glu Glu Ala Leu
20	675	685		20 865 870 875	088
	Thr Gln Lys Gly As	Thr Gln Lys Gly Asp Pro Val Ala Ile Leu Lys Arg Gln Leu Glu Glu	n Leu Glu Glu	Gln Lys Arg Leu Asp Glu Val Ser Arg Glu Leu Cys His Thr Gln Ser	n Cys His Thr Gln Ser
	069	200 200		885	895
	Lys Glu Lys Leu Let	Lys Glu Lys Leu Leu Ala Thr Glu Gln Glu Asp Ala Ala	a Val Ala Lys	Ser His Ala Ser Leu Arg Ala Asp Ala Glu Lys Ala Gln Glu Gln Gln	e Ala Gin Giu Gin Gin
	705	710 715	720	506 . 006	910

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Gln Gln Met Ala Gl	Gln Gln Met Ala Glu Leu His Ser Lys Leu Gln Ser Ser Glu Ala Glu	His Pro Pro Ala Pro Ala Glu		a Ser Lys
915	920 925	1100		ı
Val Arg Ser Lys Cy	Val Arg Ser Lys Cys Glu Glu Leu Ser Gly Leu His Gly Gln Leu Gln	Leu Arg Glu Ala Glu Glu Thr	Gln Ser Thr Leu Gln	Ala Glu Cys
930	935 940	. 1115	1120	
5 Glu Ala Arg Ala Glu	Glu Ala Arg Ala Glu Asn Ser Gln Leu Thr Glu Arg Ile Arg Ser Ile	5 Asp Gln Tyr Arg Ser Ile Leu	Ala Glu Thr Glu Gly	Met Leu Arg
945	950 960	1130	1135 1140	
Glu Ala Leu Leu Gl	Glu Ala Leu Leu Glu Ala Gly Gln Ala Arg Asp Ala Gln Asp Val Gln	Asp Leu Gln Lys Ser Val Glu	Glu Glu Glu Glu Val	Trp Arg Ala
962	5 . 970 . 975	1145	1150 1155.	
Ala Ser Gln Ala Gl	Ala Ser Gin Ala Giu Ala Asp Gin Gin Gin Thr Arg Leu Lys Giu Leu	Lys Val Gly Ala Ala Glu Glu	Glu Leu Gln Lys Ser	Arg Val Thr
10 . 980	066 586 .	. 1160	1165	
. Glu Ser Gln Val Se	Glu Ser Gln Val Ser Gly Leu Glu Lys Glu Ala Ile Glu Leu Arg Glu	Val Lys His Leu Glu	His Leu Glu Glu Ile Val Glu Lys Leu Lys Gl	Gly Glu Leu
	1000	1175	1180 1185	
Ala Val Glu Gln G	Ala Val Glu Gln Lys Val Lys Asn Asn Asp Leu Arg Glu Lys	Glu Ser Ser Asp Gln Val Arg	Glu His Thr Ser His	Leu Glu Ala
1010	1015 1020	1190	1195 1200	
15 Asn Trp Lys Ala Me	Asn Trp Lys Ale Met Glu Ale Leu Ale Thr Ale Glu Gln Ale Cys	15 Glu Leu Glu Lys His Met Ala	Ala Ala Ser Ala Glu	Cys Gln Asn
1025	1030 1035	1205	1210 1215	
Lys Glu Lys Leu L	Lys Glu Lys Leu Leu Ser Leu Thr Gln Ala Lys Glu Glu Ser Glu	. Tyr Ala Lys Glu Val Ala Gly	Leu Arg Gln Leu Leu	Leu Glu Ser
1040	1045 1050	1220	1225	
Lys Gln Leu Cys L	Lys Gln Leu Cys Leu Ile Glu Ala Gln Thr Met Glu Ala Leu Leu	Gln Ser Gln Leu Asp Ala Ala	Lys Ser Glu Ala Gln	Lys Gln Ser
20 1055	1060	20 1235 .	1240' 1245	
Ala Leu Leu Pro G.	Ala Leu Leu Pro Glu Leu Ser Val Leu Ala Gln Gln Asn Tyr Thr	Asp Glu Leu Ala Leu Val Arg	Gln Gln Leu Ser Glu	Met Lys Ser
1070	1075 1080	1250	1255 1260	
Glu Trp Leu Gln A	Glu Trp Leu Gln Asp Leu Lys Glu Lys Gly Pro Thr Leu Leu Lys	His Val Glu Asp Gly	His Val Glu Asp Gly Asp Ile Ala Gly Ala Fro Ala Se	Ser Ser Pro
1085	1090	1265	1270 1275	

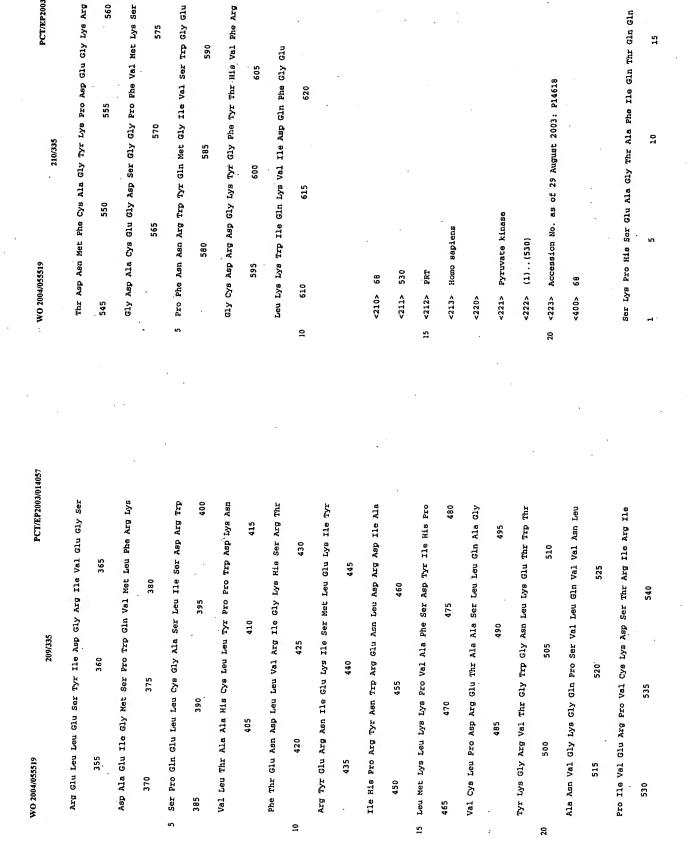
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Glu Ala Pro Pro Ala Glu Gln Asp Pro Val Gln Leu Lys Thr Gln	<2220>
1280 1285 1290	<221> Pibrinogen gamma chain precursor
Leu Glu fry Thr Glu Ala Ile Leu Glu Asp Glu Gln Thr Gln Arg	<222> (1)(453)
1295 1300 1305	<223> Accession No. as of 29 August 2003; P02679
5 Gln Lys Leu Thr Ala Glu Phe Glu Glu Ala Gln Thr Ser Ala Cys	
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Arg Leu Gln Glu Leu Glu Lys Leu Arg Thr Ala Gly Pro Leu	Met Ser Trp Ser Leu His Pro Arg Asn Leu Ile Leu Tyr Phe Tyr Ala
1325 1330 1335	1 5 10 15
Glu Ser Ser Glu Thr Glu Glu Ala Ser Gln Leu Lys Glu Arg Leu	Leu Leu Phe Leu Ser Thr Cys Val Ala Tyr Val Ala Thr Arg Asp
10 1340 1345 1350	10 20 25 30
Glu Lys Glu Lys Lys Leu Thr Ser Asp Leu Gly Arg Ala Ala Thr	Asn Cys Cys Ile Leu Asp Glu Arg Phe Gly Ser Tyr Cys Pro Thr Thr
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Arg Leu Gin Glu Leu Leu Lys Thr Thr Gin Glu Gin Leu Ala Arg	Cys Gly Ile Ala Asp Phe Leu Ser Thr Tyr Gln Thr Lys Vel Asp Lys
1370 1375 . 1380	50 55 60
15 Glu Lys Asp Thr Val Lys Lys Leu Gln Glu Gln Leu Glu Lys Ala	15 Asp Leu Gln Ser Leu Glu Asp Ile Leu His Gln Val Glu Asn Lys Thr
1385 1390 1395	. 65 70 75 80
Glu Asp Gly Ser Ser Lys Glu Gly Thr Ser Val	Ser Glu Val Lys Gln Leu Ile Lys Ala Ile Gln Leu Thr Tyr Asn Pro
1400 1405 1410	. 56 06 58
	Asp Glu Ser Ser Lys Pro Asn Met Ile Asp Ala Ala Thr Leu Lys Ser
	20 100 105 110
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<211> 453	115 120 125
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### PACT/EPP2003A Gln Lyys IIe Val Asn Leu Lys Glu Lys Val Ala Gln Leu Glu Ala Gln 145 Gln Lyys IIe Val Asn Leu Lys Glu Lys Val Ala Gln Leu Glu Ala Gln 145 150 Cys Gln Glu Pro Cys Lys Asp Thr Val Gln IIe His Asp IIe Thr Gly 165 170 180 180 180 191 195 Glu IIe Asp Gly Ser Gly Asn Gly Trp Thr Val Phe Gln Lys Arg Leu 210 215 220 230 245 245 245 246 Arg Val Glu Leu Glu Asp Trp Gly Ser Ala IIe Pro Tyr Ala Leu 246 247 248 Arg Val Glu Leu Glu Asp Trp Asn Gly Trp Thr Glu Phe Trp Leu Gly Asn Gly Asn Gly His Leu Ser Thr Gln Ser Ala IIe Pro Tyr Ala Leu 246 247 248 Arg Val Glu Leu Glu Asp Trp Asn Gly Arg Thr Ser Thr Ala Asp Tyr 248 249 Arg Val Glu Leu Glu Asp Trp Asn Gly Arg Thr Ser Thr Ala Asp Tyr 249 249 249 Arg Val Glu Leu Glu Asp Trp Asn Gly Arg Thr Ser Thr Ala Asp Tyr 249 249 249 249 240 240 240 240	14057 WO 2004/055519 PCT/RP2003/014057 206/335	Gin Phe Ser Thr Trp Asp Asn Asp Asn Asp Lys Phe Glu Gly Asn Cys	340 345 350	Ala Glu Gln Asp Gly Ser Gly Trp Met Asn Lys Cys His Ala Gly	355 360 365	5 His Leu Asn Gly Val fyr fyr Gln Gly Gly Thr fyr Ser Lys Ala Ser	370 375 380	Thr Pro Asn Gly Tyr Asp Asn Gly Ile Ile Trp Ala Thr Trp Lys Thr	385 390 395 400	Arg Trp Tyr Ser Met Lys Thr Thr Met Lys Ile Ile Pro Phe Asn	10 405 410 415	Arg Leu Thr Ile Gly Glu Gln His His Leu Gly Gly Ala Lys	420 425 430	Gln Val Arg Pro Glu His Pro Ala Glu Thr Glu Tyr Asp Ser Leu Tyr	435 440 445	15 Pro Glu Asp Asp Leu	450			<21.0> 67	20 <211> 622	<212> PRT	<213> Homo sapiens	Sec. Sec. Sec. Sec. Sec. Sec. Sec. Sec.
al Asn Leu Lya Glu Lya Val Ala G 150 150 165 170 165 170 185 170 185 187 187 187 187 187 188 188	PCT/EP2003/014057	ln Leu Glu Ala Gln	. 160	is Asp Ile Thr Gly	175	ys Gln Ser Gly Leu	190	he Leu Val Tyr Cys	205	he Gln Lys Arg Leu	20	ln Tyr Lys Glu Gly	240	he Trp Leu Gly Asn	255	le Pro Tyr Ala Leu	270	er Thr Ala Asp Tyr	285	/r Arg Leu Thr Tyr	00	ne Asp Gly Phe Asp	320	er His Asn Glv Met
al Asn Leu Lys G 150 165 165 165 18 Pro Leu Lys Asn G 245 19 Ser Gly Asn G 245 10 Ser Pro Thr G 245 10 Glu Asp Trp A 10 Glu Asp Trp A 11 Glu Asp Trp A 12 Gly Asp A 13 Gly Gly Asp A 25 C	205/335	ilu Lys Val Ala G	155	hr Val Gin Ile H	170	sn Lys Gly Ala L	185	la Asn Gln Gln P	00	ly Trp Thr Val P	i,	ys Asn Trp Ile G	235	ly Thr Thr Glu P	250	hr Gln Ser Ala I	265	an Gly Arg Thr Se	08	lu Ala Asp Lys T		la Gly Asp Ala Pi	315	vs Phe Phe Thr Se
		n Lys G	150	Lys Asp T		Ile Ala A		ro Leu Lys A	2	er Gly Asn G	215	ap Phe Lys L	230	er Pro Thr G		eu Ile Ser T		ilu Asp Trp A	12	al Gly Pro G.	295	lly Gly Asp A	310	ro Ser Asp Ly

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<400>	67				Arg Arg Gln	Glu Cys Ser Ile P	Arg Arg Gln Glu Cys Ser lle Pro Val Cys Gly Gln Asp Gln Val Thr	Gln Val Thr
					. . .	180	185	190
5 Met Al	Met Ala His Val Arg Gly Leu Gln Leu Pro Gly Cys Leu Ala Leu Ala	ceu Pro Gly Cys Leu A	ala Leu Ala		5 Val Ala Met	Thr Pro Arg Ser G	Val Ala Met Thr Pro Arg Ser Glu Gly Ser Ser Val Asn Leu Ser Pro	Leu Ser Pro
п	ហ	10	15		195		200 . 205	
Ala Le	Ala Leu Cys Ser Leu Val His Ser Gln His Val Phe Leu Ala Pro	31n His Val Phe Leu A	Ma Pro Gln		Pro Leu Glu	Gln Cys Val Pro A	Pro Leu Glu Gln Cys Val Pro Asp Arg Gly Gln Gln Tyr Gln Gly Arg	Gln Gly Arg
	20 2	25 3	30		210	. 215	220	
Gln Al	Gln Ala Arg Ser Leu Leu Gln Arg Val Arg Arg Ala Asn T	/al Arg Arg Ala Asn T	thr Phe Leu		Leu Ala Val	Thr Thr His Gly Lo	Leu Ala Val Thr Thr His Gly Leu Pro Cys Leu Ala Trp Ala Ser Ala	Ala Ser Ala
01	35 40	45			10 225	230	235	240
Glu Gl	Glu Glu Val Arg Lys Gly Asn Leu Glu Arg Glu Cys Val	Blu Arg Glu Cys Val G	Glu Glu Thr	٠	Gln Ala Lys	Ala beu Ser Lys H	Ghn Ala Lys Ala Leu Ser Lys His Gln Asp Phe Asn Ser Ala Val Gln	Ala Val Gln
50	55	09				245	250	255
Сув Se	Cys Ser Tyr Glu Glu Ala Phe Glu Ala Leu Glu Ser Ser Thr Ala Thr	ala Leu Glu Ser Ser T	thr Ala Thr	•	Leu Val Glu	Asn Phe Cys Arg A	Leu Val Glu Asn Phe Cys Arg Asn Pro Asp Gly Asp Glu Glu Gly Val	Glu Gly Val
65	. 01	75	80			260		270
15 ASD VA	Asp Val Phe Trp Ala Lys Tyr Thr Ala Cys Glu Thr Ala Arg Thr Pro	ala Cys Glu Thr Ala A	arg Thr Pro		15 Trp Cys Tyr	Val Ala Gly Lys Pa	Trp Cye Tyr Val Ala Gly Lys Pro Gly Asp Phe Gly Tyr Cys Asp Leu	Сув Авр Leu
	8 22 8 22	06	95		275	35	280 285	
Arg As	Arg Asp Lys Leu Ala Ala Cys Leu Glu Gly Asn Cys Ala Glu Gly Leu	ilu Gly Asn Cys Ala G	slu Gly Leu		Asn Tyr Cys	Glu Glu Ala Val Gl	Asn Tyr Cys Glu Glu Ala Val Glu Glu Thr Gly Asp Gly Leu Asp	Gly Leu Asp
	100	105	110		290	295	300	•
Gly Th	Gly Thr Asn Tyr Arg Gly His Val Asn Ile Thr Arg Ser Gly Ile Glu	Asn Ile Thr Arg Ser G	ily Ile Glu		Glu Asp Ser	Asp Arg Ala Ile Gl	Glu Asp Ser Asp Arg Ala Ile Glu Gly Arg Thr Ale Thr Ser Glu Tyr	Ser Glu Tyr
20	115 120	125			20 305	310	315	320
Cys 61	Cys Gln Leu Trp Arg Ser Arg Tyr Pro His Lys Pro Glu Ile Asn	ero His Lys Pro Glu I	le Asn Ser		Gln Thr Phe	Phe Asn Pro Arg Th	Gin Thr Phe Phe Asn Pro Arg Thr Phe Gly Ser Gly Glu Ala Asp Cys	Ala Asp Cys
130	135	140				325	330	335
Thr Th	Thr Thr His Pro Gly Ala Asp Leu Gin Glu Asn Phe Cys Arg Asn Pro	3in Glu Asn Phe Cys A	rg Asn Pro		Gly Leu Arg	Pro Leu Phe Glu Ly	Oly Leu Arg Pro Leu Phe Glu Lys Lys Ser Leu Glu Asp Lys Thr Glu	Lys Thr Glu
145	150	155	160			340	345	350



PCT/EP2003/01405;

*.			
	WO 2004/055519 PCT/EP2003/014057 211/335	WO 2004/055519 PCT/EP2003/014057 212/335	
	Leu His Ala Ala Met Ala Asp Thr Phe Leu Glu His Met Cys Arg Leu	Asn Leu Pro Gly Ala Ala Val Asp Leu Pro Ala Val Ser Glu Lys Asp	
	. 25 30	210 215 220	
	ABD Ile ABD Ser Pro Pro Ile Thr Ala Arg Asn Thr Gly Ile Ile Cys	Ile Gln Asp Leu Lys Phe Gly Val Glu Gln Asp Val Asp Met Val Phe	
	35 40 45	225 230 235 240	
	5 Thr lle Gly Pro Ala Ser Arg Ser Val Glu Thr Leu Lys Glu Met Ile	5 Ala Ser Phe Ile Arg Lys Ala Ser Asp Val His Glu Val Arg Lys Val	
	50 55 60	245 250 255	
	Lys Ser Gly Met Asn Val Ala Arg Leu Asn Phe Ser His Gly Thr His	Leu Gly Glu Lys Gly Lys Asn Ile Lys Ile Ile Ser Lys Ile Glu Asn	
	65 70 75 80	260 265 270	
	Glu Tyr His Ala Glu Thr Ile Lys Asn Val Arg Thr Ala Thr Glu Ser	His Glu Gly Val Arg Arg Phe Asp Glu Ile Leu Glu Ala Ser Asp Gly	
	10 85 90 95	10 275 280 285	
	Phe Ala Ser Asp Pro Ile Leu Tyr Arg Pro Val Ala Val Ala Leu Asp	Ile Met Val Ala Arg Gly Asp Leu Gly Ile Glu Ile Pro Ala Glu Lys	
	100 105 110	290 295 300	
	Thr Lys Gly Pro Glu 11e Arg Thr Gly Leu 11e Lys Gly Ser Gly Thr	Val Phe Leu Ala Gin Lys Met Met Ile Gly Arg Cys Asn Arg Ala Gly	
. '	115 120 125	305 310 315 320	
	15 Ala Glu Val Glu Leu Lys Lys Gly Ala Thr Leu Lys Ile Thr Leu Asp	15 Lys Pro Val Ile Cys Ala Thr Gln Met Leu Glu Ser Met Ile Lys Lys	
٠	130 135 140	325 330 335	
	Asn Ala Tyr Met Glu Lys Cys Asp Glu Asn Ile Leu Trp Leu Asp Tyr	Pro Arg Pro Thr Arg Ala Glu Gly Ser Asp Val Ala Asn Ala Val Leu	•
	145 150 155 160	340 345 350	
	Lys Asn lle Cys Lys Val Val Glu Val Gly Ser Lys Ile Tyr Val Asp	Asp Gly Ala Asp Cys Ile Met Leu Ser Gly Glu Thr Ala Lys Gly Asp	
	20 165 170 175	20 355 360 365	
	Asp Gly Leu Ile Ser Leu Gln Val Lys Gln Lys Gly Ala Asp Phe Leu	Tyr Pro Leu Glu Ala Val Arg Met Gln His Leu Ile Ala Arg Glu Ala	-
	180 185 190	370 375 380	
	Val Thr Glu Val Glu Asn Gly Gly Ser Leu Gly Ser Lys Lys Gly Val	Glu Ala Ala Ile Tyr His Leu Gin Leu Phe Glu Glu Leu Arg Arg Leu	
	200 205	395 395 400	

PCT/EP2003/014057				96D15	-		Leu Leu Leu Arg His	15	Pro His Gly Gln Gly	30	Pro His Asp Asp Ala	45	Leu Gly Arg Glu Val	09	Ser Gln Ala Arg Leu	08	Asp Gly Asp Gly Trp	36	His Thr Gln Gln Arg	110	Thr Tyr Asp Thr Asp	125	Asn Ala Thr Tyr Gly	140
214/335		Reticulocalbin 3 precursor		Accession No. as of 29 August 2003: Q96D15			Met Met Trp Arg Pro Ser Val Leu Leu Leu Leu Leu Leu Leu Arg His	. 10	Gly Ala Gin Gly Lys Pro Ser Pro Asp Ala Gly Pro His Gly Gln Gly	25	Arg Val His Gln Ala Ala Pro Leu Ser Asp Ala Pro His Asp Asp Ala	40	His Gly Asn Phe Gln Tyr Asp His Glu Ala Phe Leu Gly Arg Glu Val	5.5	Ala Lys Glu Phe Asp Gln Leu Thr Pro Glu Glu Ser Gln Ala Arg Leu	70 75	Gly Arg Ile Val Asp Arg Met Asp Arg Ala Gly Asp Gly Asp Gly Trp	06	Val Ser Leu Ala Glu Leu Arg Ala Trp Ile Ala His Thr Gln Gln Arg	105	His Ile Arg Asp Ser Val Ser Ala Ala Trp Asp Thr Tyr Asp Thr Asp	120	Arg Asp Gly Arg Val Gly Trp Glu Glu Leu Arg Asn Ala Thr Tyr Gly	135
WO 2004/055519	<220>	<221> Reticulocall	<2222> (1)(328)	<223> Accession No	5 <400> 69		Met Met Trp Arg Pro	н.	Gly Ala Gln Gly Ly	10 20	Arg Val His Gln Ald	35	His Gly Asn Phe Gl	0.5	15 Ala Lys Glu Phe As	65	Gly Arg Ile Val Ag	85	Val Ser Leu Ala Gl	100	His Ile Arg Asp Se	115	Arg Asp Gly Arg Va	130
057							·											~				•		
PCT/EP2003/014057	a Thr Ala Val Gly Ala Val	.0 415	a lle ile Val Leu Thr Lys	430	g Tyr Arg Pro Arg Ala Pro	445	r Ala Arg Gln Ala His Leu	460	s Asp Pro Val Gln Glu Ala	475 . 480	n Phe Ala Met Asn Val Gly	0 495	p Val Val Ile Val Leu Thr	510	n Thr Met Arg Val Val Pro	525								
. 213/335	Ala Pro Ile Thr Ser Asp Pro Thr Glu Ala Thr Ala Val	405 410	Glu Ala Ser Phe Lys Cys Cys Ser Gly Ala Ile Ile Val	420 425	Ser Gly Arg Ser Ala His Gln Val Ala Arg Tyr Arg Pro	440	ile ile Ala Val Thr Arg Asn Pro Gln Thr Ala Arg Gln	455	Tyr Arg Gly lle Phe Pro Val Leu Cys Lys Asp Pro Val	470	Trp Ala Glu Asp Val Asp Leu Arg Val Asn Phe Ala Met	485 490	Lys Ala Arg Gly Phe Phe Lys Lys Gly Asp Val Val Ile	500 505	Gly Trp Arg Pro Gly Ser Gly Phe Thr Asn Thr Met Arg	, 520					·			
WO 2004/055519	Ala Pro Ile		Glu Ala Ser		5 Ser Gly Arg	435	Ile Ile Ala	450	Tyr Arg Gly	10 465	Trp Ala Glu		Lys Ala Arg		15 Gly Trp Arg	515	. Val Pro .	. 530		20	<210> 69	<211> 328	<212> PRT	:

	WO 2004/055519	215/335	PCT/EP2003/014057	WO 2004/055519	PCT/EP2003/
	His Tyr Ala Pro Gly Glu Glu Phe His Asp Val		Glu Asp Ala Glu Thr		
	145 150	50 155	160		
	Tyr Lys Lys Met Leu Ala Arg Asp. Glu Arg Arg		Phe Arg Val Ala Asp	<210> 70	
	165	170	175	<211> 469	
	5 Gln Asp Gly Asp Ser Me	Gln Asp Gly Asp Ser Met Ala Thr Arg Glu Glu Leu Thr Ala Phe Leu	Thr Ala Phe Leu	5 <212> PRT	
	180	185	190	<213> Homo sapiens	
	His Pro Glu Glu Phe Pr	His Pro Glu Glu Phe Pro His Met Arg Asp Ile Val Ile Ala Glu Thr	Ile Ala Glu Thr	<220>	
	195	200	205	<221> Dosmin	
	Leu Glu Asp Leu Asp Ar	Leu Glu Asp Leu Asp Arg Asn Lys Asp Gly Tyr Val Gln Val Glu Glu	3ln Val Glu Glu	<222> (1)(469)	
01	210	215 220		10 <223> Accession No. as of 29 August 2003: P17661	P17661
	Tyr Ile Ala Asp Leu Ty.	Tyr Ile Ala Asp Leu Tyr Ser Ala Glu Pro Gly Glu Glu Glu Pro Ala	lu Glu Pro Ala	<400> 70	
	225 230	0 . 235	240		
	Trp Val Gln Thr Glu Arg Gln Gln Phe Arg Asp	g Gln Gln Phe Arg Asp Phe A	Phe Arg Asp Leu Asn	Ser Gln Ala Tyr Ser Ser Gln Arg Vel Ser Fyr Arg Arg Thr	r Ser Tyr Arg Arg Thr
	245	250	255		51
52		Lys Asp Gly His Leu Asp Gly Ser Glu Val Gly His Trp Val Leu Pro	rp Val Leu Pro	15 Phe Gly Gly Ala Pro Gly Phe Pro Leu Gly Ser Pro Leu Ser Ser Pro	r Pro Leu Ser Ser Pro
	260	265	270	. 20 25	30
	Pro Ala Gln Asp Gln Pro	Pro Ala Gln Asp Gln Pro Leu Val Glu Ala Asn His Leu Leu His Glu	eu Leu His Glu	Val Phe Pro Arg Ala Gly Phe Gly Ser Lys Gly Ser Ser Ser Val	Y Ser Ser Ser Val
	275	280 2	285	35 40	45
	Ser Asp Thr Asp Lys Asp	Ser Asp Thr Asp Lys Asp Gly Arg Leu Ser Lys Ala Glu Ile Leu Gly	ilu Ile Leu Gly	Thr Ser Arg Val Tyr Gin Val Ser Arg Thr Ser Gly Gly Ala Gly Gly	r Gly Gly Ala Gly Gly
20	290	300		. 50 55	. 09
	Asn Trp Asn Met Phe Val	Asn Trp Asn Met Phe Val Gly Ser Gln Ala Thr Asn Tyr Gly Glu Asp	yr Gly Glu Asp	Leu Gly Ser Leu Arg Ala Ser Arg Leu Gly Thr Thr Arg Thr Pro Ser	Thr Arg Thr Pro Ser
	305 310	315	320	25 70 75	08
	Leu Thr Arg His His Asp Glu Leu) Glu Leu		Ser Tyr Gly Ala Gly Glu Leu Leu Asp Phe Ser Leu Ala Asp Ala Val	: Leu Ala Asp Ala Val
	325			90 88	56

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WO 2004/055519	219/335	PCT/EP2003/014057	WO 2004/055519	
			Leu Arg Asn Val Val Glu Ala Gl	Leu Arg Asn Val Val Glu Ala Gln Phe Asp Ser Arg Val Arg Ala Thr
			100	105
<210> 71			Gly His Ser Tyr Glu Lys Tyr As	Gly His Ser Tyr Glu Lys Tyr Asn Lys Trp Glu Thr Ile Glu Ale Trp
<211> 417				
5 <212> PRT			5 Thr Gln Gln Val Ala Thr Glu Asr	Thr Gln Gln Val Ala Thr Glu Aen Pro Ala Leu Ile Ser Arg Ser Val
<213> Homo sapiens			130 135	140
<220>			Ile Gly Thr Thr Phe Glu Gly Arg	Ile Gly Thr Thr Phe Glu Gly Arg Ala Ile Tyr Leu Leu Lys Val Gly
<221> Carboxypeptidase B precursor	B precursor		145 . 150	155 160
<222> (1)(417)			Lys Ala Gly Gln Asn Lys Pro Als	Lys Ala Gly Gln Asn Lys Pro Ala Ils Phe Met Asp Cys Gly Phe His
10 <223> Accession No. as	Accession No. as of 29 August 2003: P15086		10 165	170 175
<400> 71			Ala Arg Glu Trp Ile Ser Pro Ale	Ala Arg Glu Trp Ile Ser Pro Ala Phe Cys Gln Trp Phe Val Arg Glu
			180	185 190
Met Leu Ala Leu Leu Val 1	Met Leu Ala Leu Leu Val Leu Val Thr Val Ala Leu Ala S	er Ala His	Ala Val Arg Thr Tyr Gly Arg Glu	Ala Val Arg Thr Tyr Gly Arg Glu Ile Gln Val Thr Glu Leu Leu Asp
1 5	10	15	. 195 200	205
is His Gly Gly Glu His Phe G	His Gly Gly Glu His Phe Glu Gly Glu Lys Val Phe Arg Val Asn Val	al Aen Val	15 Lys Leu Asp Phe Tyr Val Leu Pro	Lys Leu Asp Phe Tyr Val Leu Pro Val Leu Asn Ile Asp Gly Tyr Ile
20	25 3		210. 215	220
Glu Asp Glu Asn His Ile !	Glu Asp Glu Asn His Ile Asn Ile ile Arg Glu Leu Ala Ser Thr	er Thr Thr	Tyr Thr Trp Thr Lys Ser Arg Phe	Tyr Thr Trp Thr Lys Ser Arg Phe Trp Arg Lys Thr Arg Ser Thr His
35	45		225 230.	235 240
Gln Ile Asp Phe Trp Lys 1	Gin ile Asp Phe Trp Lys Pro Asp Ser Val Thr Gin Ile Lys Pro His	ys Pro His	Thr Gly Ser Ser Cys Ile Gly Thr	Thr Gly Ser Ser Cys lle Gly Thr Asp Pro Asn Arg Asn Phe Asp Ala
. 20 50 . 5	55 60		20 245	250 255
Ser Thr Val Asp Phe Arg V	Ser Thr Val Asp Phe Arg Val Lys Ala Glu Asp Thr Val Thr Val Glu	hr Val Glu	. Gly Trp Cys Glu ile Gly Ala Ser	Gly Trp Cys Glu Ils Gly Ala Ser Arg Asn Pro Cys Asp Glu Thr Tyr
65 70	75		260	. 265 270
Asn Val Leu Lys Gln Asn (Asn Val Leu Lys Gln Asn Glu Leu Gln Tyr Lys Val Leu I.	le Ser Asn	Cys Gly Pro Ala Ala Glu Ser Glu	Cys Gly Pro Ala Ala Glu Ser Glu Lys Glu Thr Lys Ala Leu Ala Asp
85	06	.36	275 . 280	285

Phe Ile Arg Asn Lys Leu Ser Ser Ile Lys Ala Tyr Leu Thr Ile His 290 Ser Tyr Ser Gln Met Met Ile Tyr Pro Tyr Ser Tyr Ala Tyr Lys Leu 305 5 Gly Glu Asn Asn Ala Glu Leu Asn Ala Leu Ala Lys Gly Pro Gly Ala Thr Tyr Gly Pro Gly Ala 315 Glu Leu Ala Ser Leu His Gly Thr Lys Tyr Thr Tyr Gly Pro Gly Ala 350 Thr Thr Ile Tyr Pro Ala Ala Gly Gly Ser Asp Asp Trp Ala Tyr Asp Gln Gly Ile Arg Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr Gly Arg	<pre><220> <221></pre>
315 Gly Glu Asn Asn Ala Glu Leu Asn Ala Leu Ala Lys Ala Thr Val 325 Glu Leu Ala Ser Leu His Gly Thr Lys Tyr Thr Tyr Gly Pro Gly Thr Thr Ile Tyr Pro Ala Ala Gly Gly Ser Asp Asp Trp Ala Tyr 355 Gln Gly Ile Arg Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr Gly Gly Ile Arg Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr Gly	
	Met Arg Gly Leu Leu Val Leu Ser Val Leu Leu Gly Ala Val Phe Gly 1 5 10
	Met Arg Gly Leu Leu Val Leu Ser Val Leu Leu Gly Ala Val Phe Gly 1 5 10
	1 5 10 15
	Lys Glu Asp Phe Val Gly His Gln Val Leu Arg Ile Ser Val Ala Asp
Gln Gly ile Arg Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr Gly Arg	10 20 25 30
	Glu Ala Gln Val Gln Lys Val Lys Glu Leu Glu Asp Leu Glu His Leu
370 375 380	35 40 45
Tyr Gly Phe Leu Leu Pro Glu Ser Gln Ile Arg Ala Thr Cys Glu Glu	Gln Leu Asp Phe Trp Arg Gly Pro Ala His Pro Gly Ser Pro Ile Asp
385 390 395 400	09 25 09
15 Thr Phe Leu Ala Ile Lys Tyr Val Ala Ser Tyr Val Leu Glu His Leu	15 Val Arg Val Pro Phe Pro Ser Ile Gln Ala Val Lys Ile Phe Leu Glu
405 410 415	. 65 70 75 80
Tyr	Ser His Gly Ile Ser Tyr Glu Thr Met Ile Glu Asp Vel Gln Ser Leu
	Leu Asp Glu Glu Glu Glu Gln Met Phe Ala Phe Arg Ser Arg Ala Arg
20	20 · 100 105 110
<210> 72	Ser Thr Asp Thr Phe Asn Tyr Ala Thr Tyr His Thr Leu Glu Glu Ile
<211> 419	115 120 125
<212> PRT	Tyr Asp Phe Leu Asp Leu Leu Val Ala Glu Asn Pro His Leu Val Ser
<213> Homo sapiens	130 135 140

WO 2004/055519 PCT/EP2003/014057	(014057 WO 2004/055519 PCT/EP2003/01	P2003/01
Lys lle Gln lle Gly Asn Thr Tyr Glu Gly Arg Pro lle Tyr Val Leu	. Val Thr Ala Leu Ala Ser Leu Tyr Gly Thr Lys Phe Asn Tyr Gly Ser	Ser
145 150 155 160	340 345 350	
Lys Phe Ser Thr Gly Gly Ser Lys Arg Pro Ala 11e Trp 11e Asp Thr	Ile Ile Lys Ala Ile Tyr Gln Ala Ser Gly Ser Thr Ile Asp Trp Thr	Thr
165 170 175	365 360 365	
Gly Ile His Ser Arg Glu Trp Val Thr Gln Ala Ser Gly Val Trp Phe	5 Tyr Ser Gin Gly Ile Lys Tyr Ser Phe Thr Phe Glu Leu Arg Asp Thr	Thr.
180 · 185 190	370 375 380	
Ala Lys Lys Ile Thr Gln Asp Tyr Gly Gln Asp Ala Ala Phe Thr Ala	Gly Arg Tyr Gly Phe Leu Leu Pro Ale Ser Gln Ile Ile Pro Thr Ala	Ala
200 205	385 390 395 400	400
ile Leu Asp Thr Leu Asp ile Phe Leu Glu ile Val Thr Asn Pro Asp	Lys Glu Thr Trp Leu Ala Leu Thr Ile Met Glu His Thr Leu Asn	Asn
. 210 215 220	. 10 405 410 415	
Gly Phe Ala Phe Thr His Ser Thr Asn Arg Met Trp Arg Lys Thr Arg	His Pro Tyr	
225 230 235 240		
Ser His Thr Ala Gly Ser Leu Cys Ile Gly Val Asp Pro Asn Arg Asn		
245 250 255		
Trp Asp Ala Gly Phe Gly Leu Ser Gly Ala Ser Ser Asn Pro Cys Ser	15 <210> 73	
260 265 270		
Glu Thr Tyr His Gly Lys Phe Ala Asn Ser Glu Val Glu Val Lys Ser	<212> PRT	
. 275 . 280 . 285	<213> Homo sapiens	
Ile Val Asp Phe Val Lys Asp His Gly Asn Ile Lys Ala Phe Ile Ser	<220>	
290 295 300	20 <221> Colligin 2	
lle His Ser Tyr Ser Gin Leu Leu Met Tyr Pro Tyr Gly Tyr Lys Thr	<222> (1)(418)	
305 310 315 320	<223> Accession No. as of 29 August 2003: P50454	
Glu Pro Val Pro Asp Gln Asp Glu Leu Asp Gln Leu Ser Lys Ala Ala.	<400> 73	
325 330 335		

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	WO 2004/055519 PCT/EP2003/014057 225/335	WO 2004/055519	226/335	PCT/EP2003/014057
	Met Arg Ser Leu Leu Leu Leu Ser Ala Phe Cys Leu Leu Glu Ala Ala	Glu Arg Th	Glu Arg Thr Asp Gly Ala Leu Leu Val Asn Ala Met Phe Phe Lys Pro	e Lys Pro
	1 5 10 15	3	205 200 205	
	Leu Ala Ala Glu Val Lys Ero Ala Ala Ala Ala Ala Pro Gly Thr	His Trp As	His Trp Asp Glu Lys Phe His His Lys Met Val Asp Asn Arg Gly Phe	dly Phe
	20 25 30	210	215 220	
in.	Ala Glu Lys Leu Ser Pro Lys Ala Ala Thr Leu Ala Glu Arg Ser Ala	5 Met val Th	Met Val Thr Arg Ser Tyr Thr Val Gly Val Met Met Met His Arg Thr	a Arg Thr
	35 40 45	. 225	. 230 235	. 240
	Gly Leu Ala Phe Ser Leu Tyr Gln Ala Met Ala Lys Asp Gln Ala Val	Gly Leu Ty	Gly Leu Tyr Asn Tyr Tyr Asp Asp Glu Lys Glu Lys Leu Gln Ils Val	. Ile val
	50 55 60 .		245 250	255
	Glu Asn Ile Leu Val Ser Pro Val Val Val Ala Ser Ser Leu Gly Leu	Glu Met Pr	Glu Met Pro Leu Ala His Lys Leu Ser Ser Leu Ile Ile Leu Met Pro	1 Met Pro
10	65 70 75 80	01	260 265 270	
	Val Ser Leu Gly Gly Lys Ala Thr Thr Ala Ser Gln Ala Lys Ala Val	His His Va	His His Val Glu Pro Leu Glu Arg Leu Glu Lys Leu Leu Thr Lys Glu	: Lys Glu
		275	. 280 285	
	Leu Ser Ala Glu Gln Leu Arg Asp Glu Glu Val His Ala Gly Leu Gly	Gln Leu Ly	Gln Leu Lys Ile Trp Met Gly Lys Met Gln Lys Lys Ala Val Ala Ile	. Ala Ile
	100 . 105 110	290	295 300	
15	Glu Leu Leu Arg Ser Leu Ser Asn Ser Thr Ala Arg Asn Val Thr Trp	. IS Ser Leu Pr	Ser Leu Pro Lys Gly Val Val Glu Val Thr His Asp Leu Gln Lys His	Lys His
	115 120 125	305	310 315	320
	Lys Leu Gly Ser Arg Leu Tyr Gly Pro Ser Ser Val Ser Phe Ala Asp	Leu Ala Gl	Leu Ala Gly Leu Gly Leu Thr Glu Ala Ile Asp Lys Asn Lys Ala Asp	Ala Asp
	130 135 140		325 330	335
	Asp Phe Val Arg Ser Ser Lys Gln His Tyr Asn Cys Glu His Ser Lys	Leu Ser Ar	Leu Ser Arg Met Ser Gly Lys Lys Asp Leu Tyr Leu Ala Ser Val	val Phe
20	145 150 155 160	20	340 .345 .350	,
	lle Asn Phe Arg Asp Lys Arg Ser Ala Leu Gln Ser Ile Asn Glu Trp	His Ala Th	His Ala Thr Ala Phe Glu Leu Asp Thr Asp Gly Asn Pro Phe Asp	Asp Gln
	165 170 175	. 355	5 360 365	
	Ala Ala Gin Thr Thr Asp Gly Lys Leu Pro Glu Val Thr Lys Asp Val	Asp ile Ty	Asp Ile Tyr Gly Arg Glu Glu Leu Arg Ser Pro Lys Leu Phe Tyr Ala	Tyr Ala
•	180 185 190	370	375 380	

013550/F007 OM	Fact to coordinate of		
227/335	FC (FE 2003)014037	WO 2004/055519 PCT/EP2003/014057 228/335	22
Asp His Pro Phe Ile Phe Leu Val Arg Asp Thr Gln Ser	Gln Ser Gly Ser Leu	Val Ser Leu Gln Asp Lys Thr Gly Phe His Phe Cys Gly Gly Ser Leu	
385 390 395	400	. 50 55 60	
Leu Phe Ile Gly Arg Leu Val Arg Pro Lys Gly Asp Lys	ASP LYS Met Arg Asp	ile Ser Glu Asp Trp Val Val Thr Ale Ale His Cys Gly Vel Arg Thr	
405 410	415	65 70 75 80	
Glu Leu		5 Ser Asp Val Val Val Ala Gly Glu Phe Asp Gln Gly Ser Asp Glu Glu	
		85 90	
		Asn Ile Gln Val Leu Lys Ile Ala Lys Val Phe Lys Asn Pro Lys Phe	
		100 105 110	
<210> 74		Ser Ile Leu Thr Val Asn Asn Asp Ile Thr Leu Leu Lys Leu Ala Thr	
<211> 263		10 115 120 125	
<212> PRT		Pro Ala Arg Phe Ser Gln Thr Val Ser Ala Val Cys Leu Pro Ser Ala	
<213> Homo sapiens		130 135 140	
<220>		Asp Asp Asp Phe Pro Ala Gly Thr Leu Cys Ala Thr Thr Gly Trp Gly	
<221> Chymotrypsinogen B precursor		145 150 155 160	
<222> (i) (263)		15 Lys Thr Lys Tyr Asn Ala Asn Lys Thr Pro Asp Lys Leu Gln Gln Ala	
<223> Accession No. as of 29 August 2003; P17538	17538	165 170 175	
<400> 74		Ala Leu Pro Leu Leu Ser Asn Ala Glu Cys Lys Lys Ser Trp Gly Arg	
		180 185 190	
Met Ala Phe Leu Trp Leu Leu Ser Cys Trp Ala Leu Leu Gly Thr Thr	Leu Leu Gly Thr Thr	Arg Ile Thr Asp Val Met Ile Cys Ala Gly Ala Ser Gly Val Ser Ser	
1 5 10	. 15	20 195 200 205	
Phe Gly Cys Gly Val Pro Ala Ile His Pro Val Leu Ser Gly Leu Ser	Leu Ser Gly Leu Ser	Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Gln Lys Asp Gly Ala	
20 25	30	210 215 220	
Arg Ile Val Asn Gly Glu Asp Ala Val Pro Gly Ser Trp Pro Trp Gln	Ser Trp Pro Trp Gln	Trp Thr Leu Val Gly 11e Val Ser Trp Gly Ser Agp Thr Cys Ser Thr	
35 40	455	225 230 235 240	

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Ser Ser Pro Gly Val Tyr Ala Arg Val Thr Lys Leu Ile Pro Trp Val	ile Pro Trp Val	Tyr Lys Ser Arg Ile Gln Val Arg Leu Gly Glu His Asn Ile Glu Val
245 250	255	65 70 75 80
Gln Lys Ile Leu Ala Ala Asn		Leu Glu Gly Asn Glu Gln Phe Ile Asn Ala Ays Ile Ile Arg His
. , ,		5 Pro Gln Tyr Asp Arg Lys Thr Leu Asn Asp Ile Met Leu Ile Lys
		100 105 110
<210> 75		Leu Ser Ser Arg Ala Val Ile Asn Ala Arg Val Ser Thr Ile Ser Leu
<211> 247		115 120 125
<212> PRT		Pro Thr Ala Pro Pro Ala Thr Gly Thr Lys Cys Leu Ile Ser Gly Trp
10 <213> Homo sapiens		10 130 135 140
<220>		Gly Agn Thr Ala Ser Ser Gly Ala Asp Tyr Pro Asp Glu Leu Gln Cys
<221> Trypsin I precursor		145 150 155 160
<222> (1)(247)		Leu Asp Ala Fro Val Leu Ser Gln Ala Lys Cys Glu Ala Ser Tyr Pro
<223> Accession No. as of 29 August 2003: P07477		165 170 175
15 <400> 75		15 Gly Lys Ile Thr Ser Asn Met Phe Cys Val Gly Phe Leu Glu Gly Gly
		180 185 190
Met Asn Pro Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Leu	Ala Leu Ala Ala	Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Vel Val Cys Asn Gly
1 5 10	. 15	195 200 205
Pro Phe Asp Asp Asp Lys .lle Val Gly Gly Tyr Asn Cys Glu Glu	Asn Cys Glu Glu	Gin Leu Gin Gly Val Val Ser Trp Gly Asp Gly Cys Ala Gin Lys Asn
20 20 25	30 ·	20 210 215 220
Asn Ser Val Pro Tyr Gln Vel Ser Leu Asn Ser Gly Tyr His Phe Cys	Tyr His Phe Cys	Lys Pro Gly Val Tyr Thr Lys Val Tyr Asn Tyr Val Lyg Trp 11e Lys
35 40		225 230 235 240
) Gly Gly Ser Leu Ile Asn Glu Gln Trp Val Val Ser Ala Gly His Cys	Ala Gly His Cys	Ann Thr 11e Ala Ala Asn Ser
90 25 60		245

	WO 2004/055519		PCT/EP2003/014057		WO 2004/055519		PCT/EP2003/014057
		231/335				232/335	
					Pro Lys Tyr Asn Ser Arg Th	Pro Lys Tyr Asn Ser Arg Thr Leu Asp Asn Asp Ile Leu Leu Ile Lys	ren Ile Lys
					100	105	. 011
	<210> 76				Leu Ser Ser Pro Ala Val Il	: Leu Ser Ser Pro Ala Val Ile Asn Ser Arg Val Ser Ala:Ile Ser_Leu	: Ile Ser Leu
	<211> 247	•			115	120 125	
ς.	<212> PRT	•			5 Pro Thr Ala Pro Pro Ala Al	Pro Thr Ala Pro Pro Ala Ala Gly Thr Glu Ser Leu Ile Ser Gly Trp	Ser Gly Trp
	<213> Homo sapiens			,	. 130 . 135	5 140	
	<220>				Gly Asn Thr Leu Ser Ser Gl	Gly Asn Thr Leu Ser Ser Gly Ala Asp Tyr Pro Asp Glu Leu Gln Cys	Leu Gln Cye
	<221> Trypsin II precursor	precursor			145 150	. 155	160
	<222> (1)(247)				Leu Asp Ala Pro Val Leu Se	Leu Asp Ala Pro Val Leu Ser Gln Ala Glu Cys Glu Ala Ser Tyr Pro	Ser Tyr Pro
01	<223>	Accession No. as of 29 August 2003; P07478	78		10 165	170	175
	<400> 76				Gly Lys Ile Thr Asn Asn Me	Gly Lys Ile Thr Asn Asn Met Phe Cys Val Gly Phe Leu Glu Gly Gly	glu Gly Gly
					. 180	185	
	Met Asn Leu Leu Leu	Met Asn Leu Leu Leu Ile Leu Thr Phe Val Ala Ala Ala	Ala Val Ala Ala		Lys Asp Ser Cys Gln Gly As	Lys Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Val Val Ser Asn Gly	Ser Asn Gly
	1 .55	10	15		195	200 . 205	
15	Pro Phe Asp Asp Asp	Pro Phe Asp Asp Asp Lys Ile Val Gly Gly Tyr Ile	Ile Cys Glu Glu		15 Glu Leu Gln Gly Ile Val Ser Trp Gly Tyr Gly Cys Ala Gln Lys Asn	r Trp Gly Tyr Gly Cys Ala	3ln Lys Asn
	20	25	30		210 215	5 220	
	Asn Ser Val Pro Tyr	Asn Ser Val Pro Tyr Gln Val Ser Leu Asn Ser Gly Tyr	Tyr His Phe Cys		Arg Pro Gly Val Tyr Thr Ly	Arg Pro Gly Val Tyr Thr Lys Val Tyr Asn Tyr Val Asp Trp 11e Lys	Irp 11e Lys
	35		45		225 230	235	. 240
	Gly Gly Ser Leu Ile	Gly Gly Ser Leu Ile Ser Glu Gln Trp Val Val Ser Ala	Ala Gly His Cys		Asp Thr Ile Ala Ala Asn Ser		
70	. 09.	55 60			. 245		
٠	Tyr Lys Ser Arg Ile	Tyr Lys Ser Arg ile Gin Val Arg Leu Gly Glu His Asn	Asn Ile Glu Val				
,	. 59	70 75	08				•
	Leu Glu Gly Asn Glu	Leu Glu Gly Asn Glu Gln Phe Ile Asn Ala Ala Lys Ile	Ile Ile Arg His		<210> 77	•	
	85	06	. 56		<211> 379		

	WO 2004/055519 233/335	PCT/EP2003/014057	WO 2004/055519 PC 234/335	PCT/EP2003/014057
	<212> PRT		Arg Lys Thr 11e Asn Gln Trp Val Lys Gly Gln Thr Glu Gly Lys 11e	's Ile
	<213> Homo sapiens		130 135 140	
	<2220>		Pro Glu Leu Leu Ala Ser Gly Met Val Asp Asn Met Thr Lys Leu Val	u Vel
	<221> Leukocyte elastase inhibitor (LEI)		145 . 150 . 155	160
	5 <222> (1)(379)		5 Leu Val Asn Ala Ile Tyr Phe Lys Gly Asn Trp Lys Asp Lys Phe Met	1e Met
	<223> Accession No. as of 29 August 2003: P30740	•	165 170	175
	<400> 77		Lys Glu Ala Thr Thr Asn Ala Pro Phe Arg Leu Asn Lys Lys Asp Arg	ID AEG
			180 185 190	
	Met Glu Gln Leu Ser Ser Ala Asn Thr Arg Phe Ala Leu Asp Leu Phe	p Leu Phe	Lys Thr Val Lys Met Met Tyr Gln Lys Lys Lys Phe Ala Tyr Gly Tyr	'y Tyz
	10 1 5 10	15	205 200 205	
	Leu Ala Leu Ser Glu Asn Asn Pro Ala Gly Asn Ile Phe Ile Ser Pro	e Ser Pro	Ile Glu Asp Leu Lys Cys Arg Val Leu Glu Leu Pro Tyr Gln Gly Glu	y Glu
	20 25 30		210 215 220	
	Phe Ser Ile Ser Ser Ala Met Ala Met Val Phe Leu Gly Thr Arg Gly	ir Arg Gly	Glu Leu Ser Met Val Ile Leu Leu Pro Asp Asp Ile Glu Asp Glu Ser	lu Ser
	35 . 40		225 230 235	240
	15 Asn Thr Ala Ala Gln Leu Ser Lys Thr Phe His Phe Asn Thr Val	Glu	15 Thr Gly Leu Lys Lys Ile Glu Glu Gln Leu Thr Leu Glu Lys Leu His	ou His
	50 55 60		245 250	255
	Glu Val His Ser Arg Phe Gln Ser Leu Asn Ala Asp Ile Asn Lys Arg	in Lys Arg	Glu Trp Thr Lys Pro Glu Asn Leu Asp Phe Ile Glu Val Asn. Val Ser	1 Ser
	65 70 75	. 08	260 265 270	
	Gly Ala Ser Tyr Ile Leu Lys Leu Ala Asn Arg Leu Tyr Gly Glu Lys	y Glu Lys	Leu Pro Arg Phe Lys Leu Glu Glu Ser Tyr Thr Leu Asn Ser Asp Leu	p Leu
	20 85 90	95. 20	275 280 285	
	Thr Tyr Asn Phe Leu Pro Glu Phe Leu Val Ser Thr Gln Lys Thr Tyr	18 Thr Tyr	Ala Arg Leu Gly Val Gln Asp Leu Phe Asn Ser Ser Lys Ala Asp Leu	nen di
	. 100 105 110	0;	290 295 300	
	Gly Ala Asp Leu Ala Ser Val Asp Phe Gln His Ala Ser Glu Asp Ala	u Asp Ala.	Ser Gly Met Ser Gly Ala Arg Asp Ile Phe Ile Ser Lys Ile Val His	1. His
	, 115 120 125		305 310 315	320
٠.				

	WO 2004/055519	235/335	PCT/EP2003/014057		WO 2004/055519 236/335	PCT/EP2003/01
	Lys Ser Phe Val	Lys Ser Phe Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala	Glu Ala Ala Ala		Gly Ala Asp Ala Arg Ala Leu Met Leu Gln Gly Val Asp Leu Leu Ala	d Asp Leu Leu Ala
		. 325 330	335		35 40	45
	Thr Ala Gly Ile A	Thr Ala Gly Ile Ala Thr Phe Cys Met Leu Met Pro Glu Glu Asn	Pro Glu Glu Asn Phe		Asp Ala Val Ala Val Thr Met Gly Pro Lys Gly Arg Thr	g Thr Val ile ile
	340	345	350		09 55 . 05	
" .	Thr Ala Asp His P	5 Thr Ala Asp His Pro Phe Leu Phe Phe Ile Arg His Asn Ser Ser	His Asn Ser Ser Gly		5 Glu Gln Ser Trp Gly Ser Pro Lys Val Thr Lys Asp Gly Val Thr Val	p Gly Val Thr Val
,	355	360	365		65 70 75	08
	Ser Ile Leu Phe L	Ser Ile Leu Phe Leu Gly Arg Phe Ser Ser Pro			Ala Lys Ser 11e Asp Leu Lys Asp Lys Tyr Lys Asn 11e Gly Ala Lys	n Ile Gly Ala Lys
	370	375			06 58.	95
		٠.			Leu Val Gin Asp Val Ala Asn Asn Thr Asn Glu Giu Ala Gly Asp Gly	u Ala Gly Asp Gly
10				01 ·	100	110
	<210> 78				Thr Thr Thr Ala Thr Val Leu Ala Arg Ser Ile Ala Lys Glu Gly Phe	a Lys Glu Gly Phe
	<211> 573				115 120	125
	<212> PRT				Glu Lys Ile Ser Lys Gly Ala Asn Pro Val Glu Ile Arg Arg Gly Val	e Arg Arg Gly Val
	<213> Homo sapiens	ខ្លួ			130 135 140	0
15	<220>			\$1	Met Leu Ala Val	a Lys Gln Ser Lys
•	<221> Нвр60				145 150 . 155	160
	<222> (1) (573)				Pro Val Thr Thr Pro Glu Glu Ile Ale Gln Val Ale Thr Ile Ser Ala	Thr Ile Ser Ala
	<223> Accession A	<223> Accession No. as of 29 August 2003; Pl0	. 6080		165	175
	<400> 78				Asn Gly Asp Lys Glu Ile Gly Asn Ile Ile Ser Asp Ala Met Lys Lys	Ala Met Lys Lys
70				. 50	180	190
	Met Leu Arg Leu. Pr	Met Leu Arg Leu, Pro Thr Val Phe Arg Gln Met Arg Pro Val	rg Pro Val Ser Arg		Val Gly Arg Lys Gly Val Ile Thr Val Lys Asp Gly Lys Thr	Lys Thr Leu Asn
	S E	10			195 200	205
	Val Leu Ala Pro Hi	Val Leu Ala Pro His Leu Thr Arg Ala Tyr Ala Lys Asp Val Lys Phe	ys Asp Val Lys Phe		Asp Glu Leu Glu Ile Ile Glu Gly Met Lys Phe Asp Arg Gly Tyr Ile	Arg Gly Tyr Ile
	20		30		210 215 220	

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WO 2004/055519

	WO 2004/055519	237	237/335	PCT/EP2003/014057		WO 2004/055519	238/335	PCT/EP2003/014057
	Ser Pro Tyr P	Ser Pro Tyr Phe 11e Asn Thr Ser Lys Gly Gln Lys Cys	ys Gly Gln Lys Cys	Glu Phe Gln		Lys Lys Asp Arg Val Thr Asp	Lys Lys Asp Arg Vel Thr Asp Ale Leu Asn Ale Thr Arg Ale Ale Vel	a Ala Val
	225	230	235	240		420	. 425 .430	0
	Asp Ala Tyr Va	Asp Ala Tyz Val Leu Leu Ser Glu Lys Lys Ile Ser Ser		Ile Gln Ser		Glu Glu Gly Ile Val Leu Gly	Glu Glu Gly Ile Val Leu Gly Gly Gly Cys Ala Leu Leu Arg Cys Ile	g Cys Ile
		245	250	255		435	440 445	
s		lle Val Pro Ala Leu Glu Ile Ala Asn Ala His Arg Lys		Pro Leu Val	ιn	Pro Ala Leu Asp Ser Leu Thr Pro Ala Asn Glu Asp Gln Lys Ile Gly	. Pro Ala Asn Glu Asp Gln Ly	's Ile Gly
	36	260	. 265	270	٠	450 455	460	
	Ile Ile Ala G	Ile Ile Ala Glu Asp Val Asp Gly Glu Ala Leu Ser Thr		Leu Val Leu		Ile Glu Ile Ibe Lys Arg Thr Leu Lys Ile Pro Ala Met Thr Ile Ala	Leu Lys Ile Pro Ala Met Th	r ile Ala
	275	280	285			465	475	480
	Asn Arg Leu Ly	Asn Arg Leu Lys Val Gly Leu Gln Val Val Ala Val Lys		Ala Pro Gly		Lys Asn Ala Gly Val Glu Gly Ser Leu Ile Val Glu Lys Ile Met Gln	Ser Leu Ile Val Glu Lyg·Il	e Met Gln
2	290	295	300		10	485	490	495
	Phe Gly Asp As	Phe Gly Asp Asn Arg Lys Asn Gln Leu Lys Asp Met Ala		Ile Ala Thr		Ser Ser Giu Val Gly Tyz Asp Ala Met Ala Gly Asp Phe Val Asn	Asp Ala Met Ala Gly Asp Ph	e Val Asn
	305	310	315	320		200	505 510	
	Gly Gly Ala Va	Gly Gly Ala Val Phe Gly Glu Glu Gly Leu Thr Leu Asn Leu Glu Asp	ly Leu Thr Leu Asn 1	Leu Glu Asp		Met Val Glu Lys Gly Ile Ile Asp Fro Thr Lys Val Vel Arg Thr Ala	Asp Pro Thr Lys Val Val Ar	g Thr Ala
		325	330	335		515	520 525	
51		Val Gin Pro His Asp Leu Gly Lys Val Gly Glu Val Ile Val Thr Lys	al Gly Glu Val Ile V	Val Thr Lys	15	Leu Leu Asp Ala Ala Gly Val Ala Ser Leu Leu Thr Thr Ala Glu Val	Ala Ser Leu Leu Thr Al	a Glu Val
	340		345	350		530 535	540	
	Asp Asp Ala Me	Asp Asp Ala Met Leu Leu Lys Gly Lys Gly Asp Lys Ala Gln Ile Glu	ys Gly Asp Lys Ala (sin ile Glu		Val Val Thr Glu 11e Pro Lys Glu Glu Lys Asp Pro Gly Met Gly Ala	Glu Glu Lys Asp Pro Gly Me	t Gly Ala
	355	360	365			545 550	555	260
	Lys Arg Ile Gl.	Lys Arg Ile Gin Giu Ile Ile Giu Gin Leu Asp Val Thr Thr Ser Giu	in Leu Asp Val Thr 1	thr ser Glu		Met Gly Gly Met Gly Gly Gly Met Gly Gly Gly Met Phe	Met Gly Gly Gly Met Phe	
20	370	375	380		20	565	. 570	-
	Tyr Glu Lys Gl	Tyr Glu Lys Glu Lys Leu Ann Glu Arg Leu Ala Lys Leu S	rg Leu Ala Lys Leu S	Ser Asp Gly				
	385	390	395	400				
	Val Ala Val Le	Val Ala Val Leu Lys Val Gly Gly Thr Ser Asp Val Glu V	ır Ser Asp Val Glu V	/al Asn Glu	·	<210> 79		
		405	410	415	•	<211> 803		

PCT/FEP2003001405371 **212> PRT* **221> Home septens **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (1) (803) **222> (2) August 2003; P14625 **30 *

	WO 2004/055519 241/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/0
	Pro Lys Thr Lys Lys Val Glu Lys Thr Val Trp Asp Trp Glu Leu Met	P Trp Glu Leu Met	Gin Ser Ser His His Pro Thr Asp Ile Thr Ser Leu Asp Gin Tvr Val
٠	325 330	335	515 520 525
	Asn Asp Ile Lys Pro Ile Trp Gln Arg Pro Ser Lys	Lys Glu Val Glu Glu	Lys Ile Tyr Phe
	340 345	350	530 535 540
ĸ	Asp Glu Tyr Lys Ala Phe Tyr Lys Ser Phe Ser Lys Glu Ser Asp Asp		5 Ser Arg Lys Glu Ala Glu Ser Ser Pro Phe Val Glu Arg Leu Leu Lys
	355 360		545 550 555 560
	Pro Met Ala Tyr Ile His Phe Thr Ala Glu Gly Glu Val Thr Phe Lys	1 Val Thr Phe Lys	Lys Gly Tyr Glu Val 11e Tyr Leu Thr Glu Pro Val Asp Glu Tyr Cys
	370 375 380		565 570 575
	Ser Ile Leu Phe Val Pro Thr Ser Ala Pro Arg Gly Leu	/ Leu Phe Asp Glu	lie Gin Ala Leu Pro Glu Phe Asp Gly Lys Arg Phe Gin Asn Val Ala
10	385 390 395	400	
	Tyr Gly Ser Lys Lys Ser Asp Tyr Ile Lys Leu Tyr Val Arg Arg Val	Val Arg Val	Lys Glu Gly Val Lys Phe Asp Glu Ser Glu Lys Thr Lys Glu Ser Arg
•	405 410	415	595 600 605
	Phe Ile Thr Asp Asp Phe His Asp Met Met Pro Lys	rs Tyr Leu Asn Phe	Glu Ala Val Glu Lys Glu Phe Glu Pro Leu Leu Asn Trp Met Lys Asp
	420 425	. 430	610 615 620
15	Val Lys Gly Val Val Asp Ser Asp Asp Leu Pro Leu Asn Val	Asn Val Ser Arg	Lys Ala Leu Lys Asp Lys Ile Glu Lys Ala Val Val Ser Gln Arg Leu
	435 440	445	625 630 635 640
	Glu Thr Leu Gln Gln His Lys Leu Leu Lys Val Ile	e Arg Lys Lys Leu	Thr Glu Ser Pro Cys Ale Leu Vel Ale Ser Gln Tyr Gly Trp Ser Gly
	450 455 460		645 650 655
	Val Arg Lys Thr Leu Asp Met Ile Lys Lys Ile Ala Asp Asp Lys	Asp Asp Lys Tyr	Asn Met Glu Arg Ile Met Lys Ala Gln Ala Tyr Gln Thr Gly Lys Asp
70	465 470 475	480 20	660 665 670
	Asn Asp Thr Phe Try Lys Glu Phe Gly Thr Asn Ile Lys Leu Gly Val	Lys Leu Gly Val	Ile Ser Thr Asn Tyr Tyr Ala Ser Gin Lys Lys Thr Phe Giu Ile Asn
	485 490	495	675 680 685
	rle Glu Asp His Ser Asn Arg Thr Arg Leu Ala Lys	s Leu Leu Arg Phe	Pro Arg His Pro Leu Ile Arg Asp Met Leu Arg Arg Ile Lys Glu Asp
	500 505	510 .	690 700

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	WO 2004/05S519 243/335	PCT/EP2003/014057	WO 2004/055519 244/335	PCT/EP2003/0140
	Glu Asp Asp Lys Thr Val Leu Asp Leu Ala Val Val	Val Leu Phe Glu Thr	<400> 80	
	705 710 715	720		
	Ala Thr Leu Arg Ser Gly Tyr Leu jeu Pro Asp Thr	Thr Lys Ala Tyr Gly	Met Ala Ala Ala Val Pro Arg Ala Ala Phe Leu Ser Pro Leu Leu Pro	Ser Pro Leu Leu Pro
	725	735		. 15
	5 Asp Arg Ile Glu Arg Met Leu Arg Leu Ser Leu Asn	Asn Ile Asp Pro Asp 5	Leu Leu Leu Gly Phe Leu Leu Ser Ala Pro His Gly Gly Ser Gly	His Gly Gly Ser Gly
	740 745	. 750	. 20 25 .	08
	Ala Lys Val. Glu Glu Glu Pro Glu Glu Glu Pro Glu	Glu Glu Thr Ala Glu	Leu His Thr Lys Gly Ala Leu Pro Leu Asp Thr Val Thr Phe Tyr Lys	Val Thr Phe Tyr Lys
	755 760	765	35 40	45
	Asp Thr Thr Glu Asp Thr Glu Gln Asp Glu Asp Glu	Glu Glu Met Asp Val	Val Ile Pro Lys Ser Lys Phe Val Leu Val Lys Phe Asp Thr Gln Tyr	Phe Asp Thr Gln Tyr
9	770 . 775	780 10	50 55	.09
	Gly Thr Asp Glu Glu Glu Glu Thr Ala Lys Glu Ser	Ser Thr Ala Glu Lys	Pro Tyr Gly Glu Lys Gln Asp Glu Phe Lys Arg Leu Ala Glu Asn Ser	Leu Ala Glu Asn Ser
	795 790 795	008	65 70 75	08
	Asp Glu Leu		Ala Ser Ser Asp Asp Leu Leu Val Ala Glu Val Gly Ile Ser Asp Tyr	Gly Ile Ser Asp Tyr
			85 90	9.5
15		51	Gly Asp Lys Leu Asn Met Glu Leu Ser Glu Lys Tyr Lys Leu Asp Lys	Tyr Lys Leu Asp Lys
			100 105	110
	<210> 80		Glu Ser Tyr Pro Val Phe Tyr Leu Phe Arg Asp Gly Asp Phe Glu Asn	Gly Asp Phe Glu Asn
	<211> 261		115 120	125
	<212> PRT		Pro Val Pro Tyr Thr Gly Ala Val Lys Val Gly Ala Ile Gln Arg Trp	Ala Ile Gln Arg Trp
20	<213> Homo sapiens	. 20	130 135	140
	<220>		Leu Lys Gly Gln Gly Val Tyr Leu Gly Met Pro Gly Cys Leu Pro Val	31y Cys Leu Pro Val
	<221> Endoplasmic reticulum protein ERp29 precursor (ERp31) (ERp28)	recursor (ERp31)(ERp28)	145 150 155	160
	<222> (1)(261)		Tyr Asp Ala Leu Ala Gly Glu Phe Ile Arg Ala Ser Gly Val Glu Ala	Ser Gly Val Glu Ala
	<223> Accession No. as of 29 August 2003; P30040		165 170	175

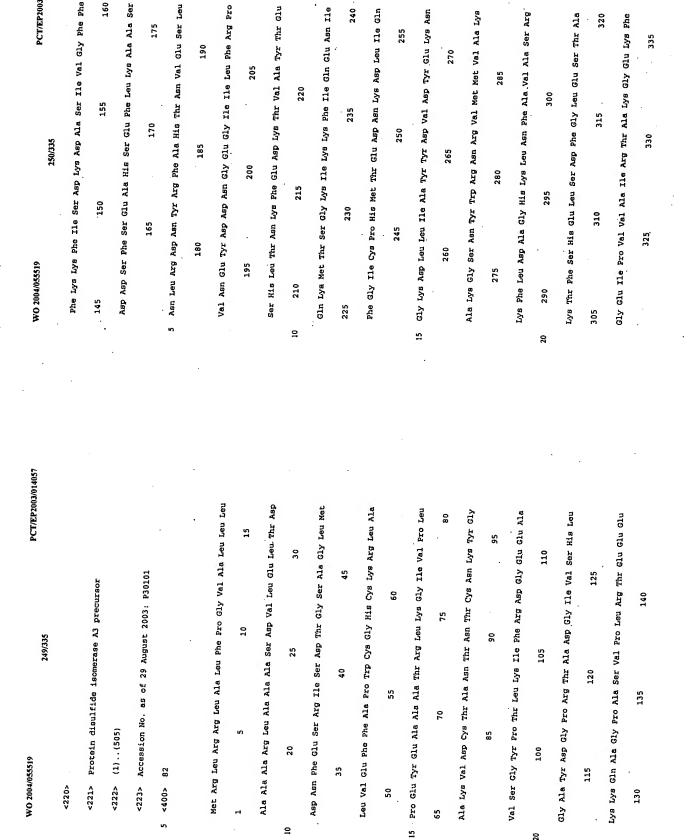
PCT/EP2003/014057

WO 2004/055519	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/01
555/547		. 246/335
Arg Gln Ala Leu Leu Lys Gln Gly Gln Asp Asn Leu Ser Ser Val Lys	Leu Ser Ser Val Lys	Met Ser Arg Gln Leu Leu Pro Val Leu Leu Leu Leu Leu Leu Arg Ala
180 . 185		1 5 10 15
Glu Thr Gln Lys Lys Trp Ala Glu Gln Tyr Leu Lys Ile Met Gly Lys	Lys lle Met Gly Lys	Ser Cys Pro Trp Gly Gln Glu Gln Gly Ala Arg Ser Pro Ser Glu Glu
195 200	205	20 25 30
i lle Leu Asp Gin Gly Glu Asp Phe Pro Ala Ser Glu Met Thr Arg Ile	Glu Met Thr Arg Ile 5	Fro Pro Glu Glu Glu Ile Pro Lys Glu Asp Gly Ile Leu Val Leu Ser
210 215	220	35 . 40 45
Ala Arg Leu Ile Glu Lys Asn Lys Met Ser Asp Gly Lys Lys Glu Glu	Gly Lys Lys Glu Glu	Arg His Thr Leu Gly Leu Ala Leu Arg Glu His Pro Ala Leu Leu Val
225 230 235	240	50 55 60
Leu Gln Lys Ser Leu Asn Ile Leu Thr Ala Phe Gln Lys Lys Gly Ala	Gln Lys Lys Gly Ala	Glu Phe Tyr Ala Pro Trp Cys Gly His Cys Gln Ala Leu Ala Pro Glu
245 250	255	
Glu Lys Glu Glu Leu		Tyr Ser Lys Ala Ala Ala Val Leu Ala Ala Glu Ser Met Val Val Thr
260	·	56 06 58
		Leu Ala Lys Val Asp Gly Pro Ala Gln Arg Glu Leu Ala Glu Glu Phe
		100 105 110
<210> 81	113	Gly Val Thr Glu Tyr Pro Thr Leu Lys Phe Phe Arg Asn Gly Asn Arg
<211> 525		115 120 125
<212> PRT		Thr His Pro Glu Glu Tyr Thr Gly Pro Arg Asp Ala Glu Gly Ile Ala
<213> Homo sapiens		130 135 140
<220>		Glu Trp Leu Arg Arg Arg Val Gly Pro Ser Ala Met Arg Leu Glu Asp
<221> Protein disulfide isomerase A2 precursor	30 z	145 150 155 160
<222> (1)(525)		Glu Aia Ala Ala Gln Ala Leu Ile Gly Gly Arg Asp Leu Val Val Ile
<223> Accession No. as of 29 August 2003: Q13087	13087	165 170. 175
<400> 81		Gly Phe Phe Gln Asp Leu Gln Asp Glu Asp Val Ala Thr Phe Leu Ala

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	WO 2004/055519		PCT/EP2003/014057	WO 2004/055519	PCT/RP3003(01
		247/335		248/335	
	Leu Ala Gln	Leu Ala Gin Asp Ala Leu Asp Met Thr Phe Gly Leu Thr Asp Arg	e Gly Leu Thr Asp Arg Pro	Trp Asp Gln Arg Pro Val Lys Thr Leu Val Gly Lys Asn Phe Glu Gln	Asn Phe Glu Gln
	195	200	205	385 390 395	007
	Arg Leu Phe	Arg Leu Phe Gin Gin Phe Gly Leu Thr Lys Asp Thr Val Val Leu Phe	8 Asp Thr Val Val Leu Phe	Val Ala Phe Asp Glu Thr Lys Asn Val Phe Val Lys Phe Tyr Ala Pro	Phe Tvr Ala Pro
	210	215	220	405 410	415
	5 Гув Гув Рhe	Lys Lys Phe Asp Glu Gly Arg Ala Asp Phe Pro Val Asp Glu Glu Leu	Pro Val Asp Glu Glu Leu	5 Trp Cys Thr His Cys Lys Glu Met Ala Pro Ala Tro Glu Ala Len ala	Glu Ala Len ala
	. 225	230	235 240	420 425	430
	Gly Leu Asp	Gly Leu Asp Leu Gly Asp Leu Ser Arg Phe Leu Val Thr His Ser Met	Leu Val Thr His Ser Met	Glu Lys Tyr Gln Asp His Glu Asp Tle Ile Ile Ala Glu Leu Asp Ala	Glu Leu Asp Ala
		245 250		435 440	445
	Arg Leu Val	Arg Leu Val Thr Glu Phe Asn Ser Gln Thr Ser Ala Lys Ile Phe Ala	Ser Ala Lys Ile Phe Ala	Thr Ala Asn Glu Leu Asp Ala Phe Ala Val His Gly Phe Pro Thr Leu	Phe Pro Thr Leu
01		260 . 265	270	10 450 455 460	
	Ala Arg Ile	Ale Arg ile Leu Asn His Leu Leu Leu Phe Val Asn Gln Thr Leu Ala	Val Asn Gln Thr Leu Ala	Lys Tyr Phe Pro Ala Gly Pro Gly Arg Lys Val Ile Glu Tyr Lys Ser	Glu Tyr Lys Ser
	275	280	285	465 470 475	680
	Ala His Arg	Ala His Arg Glu Leu Leu Ala Gly Phe Gly Glu Ala Ala Pro Arg Phe	Glu Ala Ala Pro Arg Phe	Thr Arg Asp Leu Glu Thr Phe Ser Lys Phe Leu Asp Asn Gly Gly Val	Asn Gly Gly Val
	290	295	300	485 490	495
15		Arg Gly Gln Val Leu Phe Val Val Val Asp Val Al	a Ale Asp Asn Glu	15 Leu Pro Thr Glu Glu Pro Pro Glu Glu Pro Ala Ala Pro Phe Pro Glu	ro Phe Pro Glu
	305	310	315 320		510
	His Val Leu (His Val Leu Gin Tyr Phe Gly Leu Lys Ala Giu Ala Ala Pro Thr Leu	Glu Ala Ala Pro Thr Leu	Pro Pro Ala Asn Ser Thr Met Gly Ser Lys Glu Glu Leu	ner
		325 330	335	. 515 520 5	525
	Arg Leu Val A	Arg Leu Val Asn Leu Glu Thr Thr Lys Lys Tyr Ala	Tyr Ala Pro Val Asp Gly		
20	E)	340 345	350	20	
	Gly Pro Val T	Gly Pro Val Thr Ala Ala Ser Ile Thr Ala Phe Cys	Phe Cys His Ale Val Leu	<210> 82	٠
	355	360	365	<211> 505	
	Asn Gly Gln V	Asn Gly Gln Val Lys Pro Tyr Leu Leu Ser Gln Glu	Gln Glu 11e Pro Pro Asp	-<212> PRT	
	370	375	360	<213> Homo sapiens	*

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<220>

	WO 2004/055519	251/335	PCT/EP2003/014057	WO 2004/055519 PCT 252/335	PCT/EP2003/014057
	Val Met Gln Glu G	Val Met Gln Glu Glu Phe Ser Arg Asp Gly Lys Ala Leu	u Glu Arg Phe	<210> 83	
	340	345	350	<211> 374	
	Leu Gln Asp Tyr P	Leu Gln Asp Tyr Phe Asp Gly Asn Leu Lys Arg Tyr Leu	ı Lys Ser Glu	<2125 PRT	
	355	360 365	10	<213> Homo sapiens	
	5 Pro Ile Pro Glu So	Pro Ile Pro Glu Ser Asn Asp Gly Pro Val Lys Val Val	Val Ala Glu	5 <220>	
	370	375 . 380		<221> Alcohol dehydrogenase beta chain	٠
	Asn Phe Asp Glu I.	Asn Phe Asp Glu Ile Val Asn Asn Glu Asn Lys Asp Val	. Leu lle Glu	<2222> (1)(374)	
	385	390 395	400	<223> Accession No. as of 29 August 2003: P00325	
	Phe Tyr Ala Pro Ti	Phe Tyr Ala Pro Trp Cys Gly His Cys Lys Asn Leu Glu	Pro Lys Tyr	<400> 83	
-	10 40	410	415	. 01	
	Lys Glu Leu Gly Gl	Lys Glu Leu Gly Glu Lys Leu Ser Lys Asp Pro Asn Ile	Val ile Ala	Ser Thr Ala Gly Lys Val 11e Lys Cys Lys Ala Ala Val Leu Trp Glu	7 Glu
	420	425	430	1 5 10 15	
	Lys Met Asp Ala Th	Lys Met Asp Ala Thr Ala Asn Asp Val Pro Ser Pro Tyr Glu Val Arg	Glu Val Arg	Val Lys Lys Pro Phe Ser Ile Glu Asp Val Glu Val Ala Pro Pro Lys	о 1.ув
	435	440 445		20 25 30	
15		Gly Phe Pro Thr 11e Tyr Phe Ser Pro Ala Asn Lys Lys Leu Asn Pro	Leu Asn Pro	5 Ala Tyr Glu Val Arg Ile Lys Met Val Ala Val Gly Ile Cys Arg Thr	g Thr
	450	455 460		35 40 . 45	
	Lys Lys Tyr Glu 61	Lys Lys Tyr Glu Gly Gly Arg Glu Leu Ser Asp Phe Ile S	Ser Tyr Leu	Asp Asp His Val Val Ser Gly Asm Leu Val Thr Pro Leu Pro Val Ile	l Ile
	465	470 475	480	90 25 09	
	Gln Arg Glu Ala Th	Gln Arg Glu Ala Thr Asn Pro Pro Val Ile Gln Glu Glu Lys Pro Lys	Lys Pro Lys	Leu Gly His Glu Ala Ala Gly Ile Val Glu Ser Val Gly Glu Gly Val	val
, 72	20 485	5 490	495	65 70 75	80
	Lys Lys Lys Ala Gln Glu Asp Leu	a Gln Glu Asp Leu		Thr Thr Val Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Thr Pro Gln	· Gln ·
	200	. 505		. Se 06 58	

Cys Gly Lys Cys Arg Val Cys Lys Asn Pro Glu Ser Asn Tyr Cys Leu

. WO 2004/055519 PCT/EP2003/014057	Pro Met Leu Leu Thr Gly Arg Thr Trp Lys Gly Ala Val Tyr Gly	305 310 315 - 320	Gly Phe Lys Ser Lys Glu Gly Ile Pro Lys Leu Val Ala Asp Phe Met	325 330 335	5 Ala Lys Lys Phe Ser Leu Asp Ala Leu Ile Thr His Val Leu Pro Phe	340 345 350	Glu Lys Ile Asn Glu Gly Phe Asp Leu Leu His Ser Gly Lys Ser Ile	355 360 365	Arg Thr Val Leu Thr Phe	10 370			<210> 84	<211> 241	15 <212> PRT	<213> Homo sapiens	<220>	<221> Glutathione transferase omega 1	<222> (1)(241)	20 <223> Accession No. as of 29 August 2003: P78417	<400> 84		Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro	1 5 10 15
WO 2004/055519 PCT/EP2003/014057 253/335	Lys Asn Asp Leu Gly Asn Pro Arg Gly Thr Leu Gln Asp Gly Thr Arg	115 120 125	Arg Phe Thr Cys Arg Gly Lys Pro 11s His His Phe Leu Gly Thr Ser	130 135 140	5 Thr Phe Ser Gln Tyr Thr Val Val Asp Glu Asn Ala Val Ala Lys Ile	145 150 155 160	Asp Ala Ala Ser Pro Leu Glu Lys Val Cys Leu Ile Gly Cys Gly Phe	165 170 175	Ser Thr Gly Tyr Gly Ser Ala Val Asn Val Ala Lys Val Thr Pro Gly	10 180 185 190	Ser Thr Cys Ala Val Phe Gly Leu Gly Gly Val Gly Leu Ser Ala Val	200 205	Met Gly Cys Lys Ala Ala Gly Ala Ala Arg Ile Ile Ala Val Asp Ile	210 215 220	15 Asn Lys Asp Lys Phe Ala Lys Ala Lys Glu Leu Gly Ala Thr Glu Cys	225 230 235 240	ile Asn Pro Gln Asp Tyr Lys Lys Pro Ile Gln Glu Val Leu Lys Glu	. 250 255	Met Thr Asp Gly Gly Val Asp Phe Ser Phe Glu Val Ile Gly Arg Leu	20 260 265 270	Asp Thr Met Met Ala Ser Leu Leu Cys Cys His Glu Ala Cys Gly Thr	275 280 . 285	Ser Val Ile Val Gly Val Pro Pro Ala Ser Gln Asn Leu Ser Ile Asn	290 295 300

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Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys	rg Phe Cys	Asp Pro Thr Val Ser Al	Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly	o Try Gln Gly
. 20 25 30	0	210	215 220	•
Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg	ly ile Arg	Phe Leu Glu Leu Tyr Le	Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly	s Asp Tyr Gly
35 40 45		225	230 235	240
His Glu Val ile Asn ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe	. She Phe	Leu		
55 60				
Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly	er Gln Gly			
65 70 75	. 08			
Gin Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala	sp Glu Ala	<210> 85		
. 06	95			
Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys	ys Ala Cys	<212> PRT		
100 105	110	<213> Homo sapiens		
Gin Lys Wet Ile Leu Giu Leu Phe Ser Lys Val Pro Ser Leu Val Gly	eu Val Gly	<220>		
115 120 125		<221> 150 kDa oxygen-	150 kDa oxygen-regulated protein precursor (Orpl50)	(Orp150)
Ser Phe ile Arg Ser Gin Asn Lys Glu Asp Tyr Ala Gly Le	eu Lys Glu	<222>		¥ .
130 135 140		<223> Accession No. 8	Accession No. as of 29 August 2003: Q9Y4L1	
Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Glu Val Leu Thr Asn Lys	hr Asn Lys	<400> 85		
145 150 155				
Lye Thr Thr Phe Phe Gly Gly Asm Ser Ile Ser Met Ile Asp Tyr Leu	sp Tyr Leu	Met Ala Asp Lys Val An	Met Ala Asp Lys Val Arg Arg Gln Arg Pro Arg Arg Arg Val Cys Trp	y Val Cys Trp
165 1,0	175 20		. 10	
Ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys	sn dlu Cys	Ala Leu Val Ala Val Le	Ala Leu Val Ala Val Leu Leu Ala Asp Leu Leu Ala Leu Ser Asp Thr	Ser Asp Thr
180 . 185 . 190	06	. 50	25	30
Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu	et Lys Glu	Leu Ala Val Met Ser Va	Leu Ala Val Met Ser Val Asp Leù Gly Ser Glu Ser Met Lys Val Ala	: Lys Val Ala
195 200 205		35	40	

	WO 2004/055519	257/335	PCT/EP2003/014057	WO 2004/055519 ·	PCT/EP2003/01
	Ile Val Lys Pro Gl3	ile Val Lys Pro Gly Val Pro Met Glu ile Val Leu Asn Lys Glu	al Leu Asn Lys Glu Ser	Thr 11e Val Thr Tyr Gln Met Val Lys Thr Lys Glu Ala Gly Met Gln	la Gly Met Gln
	20		. 09	245 250	255
	Arg Arg Lys Thr Pro	Arg Arg Lys Thr Pro Val Ile Val Thr Leu Lys Glu Asn Glu Arg Phe	ys Glu Asn Glu Arg Phe	Pro Gln Leu Gln Ile Arg Gly Val Gly Phe Asp Arg Thr Leu Gly Gly	hr Leu Gly Gly
	65	70 . 75	90	260 265	270
	5 Phe Gly Asp Ser Ala	Phe Gly Asp Ser Ala Ala Ser Met Ala Ile Lys Asn Pro Lys Ala Thr	ys Asn Pro Lys Ala Thr	5 Leu Glu Met Glu Leu Arg Leu Arg Glu Arg Leu Ala Gly Leu Phe Asn	ly Leu Phe Asn
	85	06		275 280 2	
	Leu Arg Tyr Phe Gln	Leu Arg Tyr Phe Gln His Leu Leu Gly Lys Gln Ala Asp Asn Pro His	In Ala Asp Asn Pro His	Glu Gln Arg Lys Gly Gln Arg Ala Lys Asp Val Arg Glu Asn Pro Arg	lu Asn Pro Arg
	100	105	110	290 295 300	
	Val Ala Leu Tyr Gln	Val Ala Leu Tyr Gin Ala Arg Phe Pro Giu His Giu Leu Thr Phe Asp	is Glu Leu Thr Phe Asp	Ala Met Ala Lys Leu Leu Arg Glu Ala Asn Arg Leu Lys Thr Val Leu	ys Thr Val Leu
2	115	120	125	10 305 310 315	. 320
	Pro Gln Arg Gln Thr	Pro Gin Arg Gin Thr Val His Phe Gin Ile Ser Ser Gin Leu Gin Phe	er Ser Gln Leu Gln Phe	Ser Ala Asn Ala Asp His Met Ala Gin Ile Glu Gly Leu Met Asp Asp	eu Met Asp Asp
	130	135	140	325 . 330	335
	Ser Pro Glu Glu Val	Ser Pro Glu Glu Val Leu Gly Met Val Leu Asn Tyr Ser Arg Ser Leu	sn Tyr Ser Arg Ser Leu	Val Asp Phe Lys Ala Lys Val Thr Arg Val Glu Phe Glu Glu Leu Cys	lu Glu Leu Cys
	145	150 155	160	340 . 345	350
51		Ala Glu Asp Phe Ala Glu Gln Pro Ile Lys Asp Al	op Ala Val Ile Thr Val	15 Ala Asp Leu Phe Glu Arg Val Pro Gly Pro Val Gln Gln Ala Leu Gln	in Ala Leu Gln
	165	170	175	355	365
	Pro Val Phe Phe Asn	Pro Val Phe Phe Asn Gln Ala Glu Arg Arg Ala Val Leu Gln Ala Ala	a Val Leu Gln Ala Ala	Ser Ala Glu Met Ser Leu Asp Glu Ile Glu Gln Val Ile Leu Val Gly	le Leu Val Gly
	180	185	190	370 375 380	
	Arg Met Ala Gly Leu	Arg Met Ala Gly Leu Lys Val Leu Gln Leu Ile Asn Asp Asn	е Авп Авр Авп Тhr Ala	Gly Ala Thr Arg Val Pro Arg Val Gln Glu Val Leu Leu Lys Ala Val	eu Lys Ala Val
20	195	. 200		20 385 390 395	400
	Thr Ala Leu Ser Tyr	Thr Ala Leu Ser Tyr Gly Val Phe Arg Arg Lys Asp Ile Asn Thr Thr	's Asp Ile Asn Thr Thr	Gly Lys Glu Glu Leu Gly Lys Asn Ile Asn Ala Asp Glu Ala Ala Ala	lu Ala Ala Ala
	210	215		405 - 410	415
	Ala Gin Asn Ile Met	Ala Gin Asn ile Met Phe Tyr Asp Met Gly Ser Gly Ser Thr Val Cys	r Gly Ser Thr Val Cys	Met Gly Ale Val Tyr Gln Ala Ala Ala Leu Ser Lys Ale Phe Lys Val	la Phe Lys Val
	225	230 235	5 240	420 . 425	430

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Lys Pro Phe Val Val Arg Asp Ala Val Val Tyr Pro 11e Leu Val Glu	Glu Ala Glu Ala Pro Val Glu Asp Gly Ser Gln Pro Pro Pro Pro Glu
435 440 445	625 630 635 640
Phe Thr Arg Glu Val Glu Glu Glu Pro Gly Ile His Ser Leu Lys His	Pro Lys Gly Asp Ala Thr Pro Glu Gly Glu Lys Ala Thr Glu Lys Glu
. 450 455 460 .	645 650 655
5 Asn Lys Arg Val Leu Phe Ser Arg Met Gly Pro Tyr Pro Gln Arg Lys	5 Asn Gly Asp Lys Ser Glu Ala Gln Lys Pro Ser Glu Lys Ale Glu Ale
465 470 475 480	019
Val Ile Thr Phe Asn Arg Tyr Ser His Asp Phe Asn Phe His Ile Asn	Gly Pro Glu Gly Val Ala Pro Ala Pro Glu Gly Glu Lys Lys Gln Lys
485 490 495	675 680 685
Tyr Gly Asp Leu Gly Phe Leu Gly Pro Glu Asp Leu Arg Val Phe Gly	Pro Ala Arg Lys Arg Arg Met Val Glu Glu Ile Gly Val Glu Leu Val
.0 500 505 510	10 690 695 700
Ser Gin Asn Leu Thr Val Lys Leu Lys Gly Val Gly Asp Ser Phe	Val Leu Asp Leu Pro Asp Leu Pro Glu Asp Lys Leu Ala Gln Ser Val
515 520 525	705 710 715 720
Lys Lys Tyr Pro Asp Tyr Glu Ser Lys Gly Ile Lys Ala His Phe Asn	Gln Lys Leu Gln Asp Leu Thr Leu Arg Asp Leu Glu Lys Gln Glu Arg
530 535 540	. 725 . 730 . 735
5 Leu Asp Glu Ser Gly Val Leu Ser Leu Asp Arg Val Glu Ser Val Phe	is Glu Lys Ala Ala Asn Ser Leu Glu Ala Phe Ile Phe Glu Thr Gln Asp
545 550 555	740 745 750
Glu Thr Leu Val Glu Asp Ser Ala Glu Glu Glu Ser Thr Leu Thr Lys	Lys Leu Tyr Gln Fro Glu Tyr Gln Glu Val Ser Thr Glu Glu Gln Arg
565 570 575	755 760 765
Leu Gly Aen Thr Ile Ser Ser Leu Phe Gly Gly Gly Thr Thr Pro Asp	Glu Glu 11e Ser Gly Lys Leu Ser Ala Ala Ser Thr Trp Leu Glu Asp
0 580 585 590	20 770 775 780
Ale Lys Glu Asn Gly Thr Asp Thr Vel Gln Glu Glu Glu Ger Pro	Glu Gly Val Gly Ala Thr Thr Val Met Leu Lys Glu Lys Leu Ala Glu
595 600 605	785 790 795 800
Ala Glu Gly Ser Lys Asp Glu Pro Gly Glu Gln Val Glu Leu Lys Glu	Leu Arg Lys Leu Cys Gln Gly Leu Phe Phe Arg Val Glu Glu Arg Lys
610 615 620	805 810 815

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•	Glu Phe Lys Glu Leu Lys Leu Thr Asp Tyr Arg Gly Lys	Asp Tyr Arg Gly Lys Tyr Leu Val	<210> 87
	100	105	<211> 288
	Phe Phe Phe Tyr Pro Leu Asp Phe Thr Phe Val Cys Pro	Thr Phe Val Cys Pro Thr Glu Ile	<212> PRT
	115 120	125	<213> Homo sapiens
ĸ	Ile Ala Phe Gly Asp Arg Leu Glu Glu Phe Arg Ser Ile	Asn Thr Glu	5 <220>
	130 135		<221> MAWD binding protein
	Val Val Ala Cys Ser Val Asp Ser Gln Phe Thr His Leu	Gln Phe Thr His Leu Ala Trp Ile	<222> (1)(288)
	145 150	155	<223> Accession No. as of 29 August 2003: P30039
	Asn Thr Pro Arg Arg Gln Gly Gly Leu Gly Pro 11e Arg	Leu Gly Pro ile Arg ile Pro Leu	<400> 87
01	165	170 . 175	
	Leu Ser Asp Leu Thr His Gln Ile Ser Lys Asp Tyr Gly	Ser Lys Asp Tyr Gly Val Tyr Leu	Met Lys Leu Pro Ile Phe Ile Ala Asp Ala Phe Thr Ala Arg Ala Phe
	. 180	185 190	. 5 . 10 . 15
	Glu Asp Ser Gly His Thr Leu Arg Gly Leu Phe Ile Ile	Gly Leu Phe Ile Ile Asp Asp Lys	Arg Gly Asn Pro Ala Ala Val Cys Leu Leu Glu Asn Glu Leu Asp Glu
	195 200	205	20 25 30
15	Gly ile Leu Arg Gln ile Thr Leu Asn Asp Leu Pro Val	Asn Asp Leu Pro Val Gly Arg Ser	Asp Met His Gln Lys Ile Ala Arg Glu Met Asn Leu Ser Glu Thr Ala
	210 215	220	35 40 45
	Val Asp Glu Thr Leu Arg Leu Val Gln Ala Phe Gln Tyr	Sin Ale Phe Gin Tyr Thr Asp Lys	Phe lle Arg Lys Leu His Pro Thr Asp Asn Phe Ala Gln Ser Ser Cys
	225 230	235 240	20 55 60
	His Gly Glu Val Cys Pro Ala Gly Trp Lys Pro Gly Ser	Irp Lys Pro Gly Ser Glu Thr Ile	Phe Gly Leu Arg Try Phe Thr Pro Ala Ser Glu Val Pro Leu Cys Gly
20	245	250 255 20	65 70 75 80
	Ile Pro Asp Pro Ala Gly Lys Leu Lys Tyr Phe Asp Lys	Lys Tyr Phe Asp Lys Leu Asn	His Ala Thr Leu Ala Ser Ala Ala Val Leu Phe His Lys Ile Lys Asn
	260 2	265 270 .	56. 06
			Met Asn Ser Thr Leu Thr Phe Val Thr Leu Ser Gly Glu Leu Arg Ala

	WO 2004/055519	265/335	PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057	<u>.</u>
	Arg Arg Ala Glu Asp Gly Ile Val Leu Asp Leu Pro Leu	e Val Leu Asp Leu Pro Leu	Tyr Pro Ala	<210> 88	
	115	120 . 125		<211> 511	
	His Pro Gln Asp Phe His Glu Val Glu Asp Leu Ile Lys	u Val Glu Asp Leu Ile Lys	Thr Ale Ile	<212> PRT	
	130 135	5	÷,	<213> Homo sapiens	
'n	Gly Asn Thr Leu Val Gln Asp Ile Cys Tyr Ser Pro Asp		Thr Gln Lys	5 <220>	
	145 150	155.	. 160	<221> Alpha-amylase 2B precursor	
	Leu Leu Val Arg Leu Ser Asp Val Tyr Asn Arg Ser Phe		Leu Glu Asn	<222> (1) (511)	
	165	170	175	<223> Accession No. as of 29 August 2003; P19961	
•	Leu Lys Val Asn Thr Glu Asn Leu Leu Gln Val	Glu Asn	Thr Gly Lys	<400> 88	
21	180	185			
•	Val Lys Gly Leu Ile Leu Thr Leu Lys Gly Glu Pro Gly		Gly Gln Thr	Met Lys Phe Phe Leu Leu Ehe Thr Ile Gly Phe Cys Try Ala Gln	
	195	200 205		1 5 10 15	
•	Gln Ala Phe Asp Phe Tyr Ser Arg Tyr Phe Ala Pro Trp		Val Gly Val	Tyr Ser Pro Asn Thr Gln Gln Gly Arg Thr Ser 11e Val His Leu Phe	
	210 215	220		20 25 30	
15	Ala Glu Asp Pro Val Thr Gly Ser Ala His Ala Val Leu		Ser Ser Tyr	15 Glu Trp Arg frp Val Asp Ile Ala Leu Glu Cye Glu Arg Tyr Leu Ala	
	225 230	235	240	35 40 45	
	Trp Ser Gin His Leu Gly Lys Lys Glu Met His Ala Phe		Gln Cys Ser	Pro Lys Gly Phe Gly Gly Val Gln Val Ser Pro Pro Asn Glu Asn Val	
	245	250		. 50 55 60	
	His Arg Gly Glu Leu Gly Ile Ser Leu Arg Pro Asp		Gly Arg Val	Ala ile His Asn Pro Phe Arg Pro Trp Trp Glu Arg Tyr Gln Pro Val	
8	260	. 265	270	20 65 70 75 80	
	Asp Ile Arg Gly Gly Ala Ala Val Val Leu Glu Gly Thr		Leu Thr Ala	Ser Tyr Lys Leu Cys Thr Arg Ser Gly Asn Glu Asp Glu Phe Arg Asn	
	275	280 285		85	
				. Met Val Thr Arg Cys Asn Asn Val Gly Val Arg Ile Tyr Vel Asp Ale	

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Val Ile Asn His Met Ser Gly Asn Ala Vel Ser Ala Gly Thr Ser Ser	Asp Arg Ala Leu Val Phe Val Asp Asn His Asp Asn Gln Arg Gly His
115 120 125	. 305 310 315 320
Thr Cys Gly Ser Tyr Phe Asn Pro Gly Ser Arg Asp Phe Pro Ala Val	Gly Ala Gly Ala Ser Ile Leu Thr Phe Trp Asp Ala Arg Leu Tyr
130 . 135 140 .	325 330 335
5 Pro Tyr Ser Gly Trp Asp Phe Asn Asp Gly Lys Cys Lys Thr Gly Ser	5 Lys Met Ala Val Gly Phe Met Leu Ala His Pro Tyr Gly Phe Thr Arg
145 150 155 160	340 345 350
Gly Asp Ile Glu Asn Tyr Asn Asp Ala Thr Gln Val Arg Asp Cys Arg	Val Met Ser fyr Arg Trp Pro Arg Gln Phe Gln Asn Gly Asn Asp
165 170 175	355 360 365
Leu Val Gly Leu Leu Asp Leu Ala Leu Glu Lys Asp Tyr Val Arg Ser	Val Asn Asp Trp Val Gly Pro Pro Asn Asn Asn Gly Val 11e Lys Glu
10 180 185 190	10 370
Lys lle Ala Glu Tyr Met Asn His Leu Ile Asp Ile Gly Val Ala Gly	Val Thr Ile Asn Pro Asp Thr Thr Cys Gly Asn Asp Trp Val Cys Glu
195 200. 205	385 390 395 400
Phe Arg Leu Asp Ala Ser Lys His Met Trp Pro Gly Asp Ile Lys Ala	His Arg Trp Arg Gln Ile Arg Asn Met Val Asn Phe Arg Asn Val Val
210 215 220	405 410 415
15 Ile Leu Asp Lys Leu His Asn Leu Asn Ser Asn Trp Phe Pro Ala Gly	is Asp Gly Gln Pro Phe Thr Asn Try Tyr Asp Asn Gly Ser Asn Gln Vel
225 230 ,235 240	420 425 430
Ser Lys Pro Phe Ile Tyr Gln Glu Val Ile Asp Leu Gly Gly Glu Pro	Ala Phe Gly Arg Gly Asn Arg Gly Phe Ile Val Phe Asn Asn Asp Asp
245 250 255	435 440 445
Ile Lys Ser Asp Tyr Phe Gly Asn Gly Arg Val Thr Glu Phe Lys	Trp Thr Phe Ser Leu Thr Leu Gln Thr Gly Leu Pro Ala Gly Thr Tyr
20 260 265 . 270	20 450 455 460
Tyr Gly Ale Lys Leu Gly Thr Vel Ile Arg Lys Trp Asn Gly Glu Lys	Cys Asp Val 11e Ser Gly Asp Lys 11e Asn Gly Asn Cys Thr Gly 11e
275 280 285	465 470 475 480
Met Ser Tyr Leu Lys Asn Trp Gly Glu Gly Trp Gly Phe Met Pro Ser	Lys lle Tyr Val Ser Asp Asp Gly Lys Ala His Phe Ser Ile Ser Asn
. 300 . 295	. 495

PCT/EP2003/014057 15 Met Lys Phe Phe Leu Leu Phe Thr Ile Gly Phe Cys Trp Ala Gln Tyr Ser Pro Asn Thr Gln Gln Gly Arg Thr Ser Ile Val His Leu Phe Glu Trp Arg Trp Val Asp Ile Ala Leu Glu Cys Glu Arg Tyr Leu Ala Pro Lys Gly Phe Gly Gly Val Gln Val Ser Pro Pro Asn Glu Asn Val Ala ile Tyr Asn Pro Phe Arg Pro Trp Trp Glu Arg Tyr Gln Pro Val 80 Ser Ala Glu Asp Pro Phe Ile Ala Ile His Ala Glu Ser Lys Leu 510 30 <223> Accession No. as of 29 August 2003: P04746 9 <221> Alpha-amylase, pancreatic precursor 10 505 52 \$ 22 Homo sapiens <222> (1)..(511) 200 <211> 511 <212> PRT 83 35 83 <210> <213> <400>> <220> 20

2

5 Val Ile Asn His Met Cys Gly Asn Ala Val Ser Ala Gly Thr Ser Ser Met Val Thr Arg Cys Asn Asn Val Gly Val Arg Ile Tyr Val Asp Ale Thr Cys Gly Ser Tyr Phe Asn Pro Gly Ser Arg Asp Phe Pro Ala Val Gly Asp Ile Glu Asn Tyr Asn Asp Ala Thr Gln Val Arg Asp Cys Arg Pro Tyr Ser Gly Trp Asp Phe Asn Asp Gly Lys Cys Lys Thr Gly Ser Leu Thr Gly Leu Leu Asp Leu Ala Leu Glu Lys Asp Tyr Val Arg Ser 15 Lys lle Ala Glu Tyr Met Asn His Leu Ile Asp Ile Gly Val Ala Gly Phe Arg Leu Asp Ala Ser Lys His Met Trp Pro Gly Asp Ile Lys Ala Ile Leu Asp Lys Leu His Asn Leu Asn Ser Asn Trp Phe Pro Ala Gly 240 Ser Lys Pro Phe 11e Tyr Gln Glu Val 11e Asp Leu Gly Gly Glu Pro 175 110 125 205 140 155 235 170 105 185 120 200 135 215 150 230 165 100 180 115 195 130 210 10 145 225

ile Lys Ser Ser Asp Tyr Phe Gly Asn Gly Arg Val Thr Glu Phe Lys

250

245

2

270

265

260

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Ser Tyr Lys Leu Cys Thr Arg Ser Gly Asn Glu Asp Glu Phe Arg Asn

90

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Tyr Gl	y Ala Lys Leu Gl	Tyr Gly Ala Lys Leu Gly Thr Val Ile Arg Lys Trp Asn	Lys Trp Asn Gly	Gly Glu Lys			Cys Asp V	al Ile Ser Gly Asp	Cys Asp Val Ile Ser Gly Asp Lys Ile Asn Gly Asn Cys Thr Gly Ile	sn Cys Thr Gly Ile
•	275	280	. 285				465	470	475	480
Met Se	r Tyr Leu Lys As	Met Ser Tyr Leu Lys Asn Trp Gly Glu Gly Trp Gly Phe		Val Pro Ser			Lys Ile 1	yr Val Ser Asp Asp	Lys ile Tyr Vel Ser Asp Asp Gly Lys Ala His Phe Ser Ile Ser Asn	10 Ser Ile Ser Asn
290	0.	295	300					485	490	495
5 ABD Ar	g Ala Leu Val Ph	Asp Arg Ala Leu Val Phe Val Asp Asn His Asp Asn Gln		Arg Gly His		'n		ilu Asp Pro Phe Ile	Ser Ala Glu Asp Pro Phe Ile Ala Ile His Ala Glu Ser Lys Leu	iu Ser Lys Leu
305	310		315	320				200	505	510
Gly Al	a Gly Gly Ala Se	Gly Ala Gly Gly Ala Ser Ile Leu Thr Phe Trp Asp Ala		Arg Leu Tyr						
	325	330		335						
Lyв Ме	t Ala Val Gly Ph	Lys Met Ala Val Gly Phe Met Leu Ala His Pro Tyr Gly		Phe Thr Arg			<210> 90	ų.		
01	. 340	345	350			10	<211> 553	e ·		
Val Me	t Ser Ser Tyr Ar	Val Met Ser Tyr Arg Trp Pro Arg Gln Phe Gln Asn Gly Asn Asp	Phe Gln Asn Gly	Asn Asp			<212> PRT	Ē;		
	355	360	365				<213> Ho	<213> Homo sapiens		
Val As	n Asp Trp Val Gl	Val Asn Asp Trp Val Gly Pro Pro Asn Asn Asn Gly Val Ile Lys Glu	Asn Gly Val Ile	Lys Glu			<220>			
370	0	375.	380				<221> AT	ATP synthase alpha chain	hain	
15 Val Thi	r Ile Asn Pro ABI	Val Thr Ile Asn Pro Amp Thr Thr Cys Gly Asn Asp Trp V	Asn Asp Trp Val	/al Cys Glu		15	<222>	(1)(553)		
385	390		395	400			<223> Ac	cession No. as of	Accession No. as of 29 August 2003; P25705	705
His Ar	g Trp. Arg Gln Ile	His Arg Trp.Arg Gln Ile Arg Asn Met Val Ile Phe Arg Asn Val Val	lle Phe Arg Asn	Val Val			<400>>			
	405	410		415						
Asp Gli	y Gln Pro Phe Th	Asp Gly Gln Pro Phe Thr Asn Trp Tyr Asp Asn Gly Ser Asn Gln Val	ksn Gly Ser Asn	Gln Val			Met Leu S	er Val Arg Val Ale	Met Leu Ser Val Arg Val Ala Ala Val Val Arg Ala Leu Pro Arg	g Ala Leu Pro Arg
20	420	425	430			20	ч	ហ	10	15
Ala Phe	e Gly Arg Gly Ası	Ala Phe Gly Arg Gly Aen Arg Gly Phe Ile Val Phe Asn Asn Asp Asp	al Phe Asn Asn	Азр Азр			Arg Ala G	ly Leu Val Ser Arg	Arg Ala Gly Leu Val Ser Arg Asn Ala Leu Gly Ser Ser Phe Ile Ala	r Ser Phe Ile Ala
	435	440	445					20	25	30
Trp Sea	r Phe Ser Leu Th	Trp Ser Phe Ser Leu Thr Leu Gln Thr Gly Leu Pro Ala Gly Thr Tyr	en Pro Ala Gly	Thr Tyr			Ala Arg A	sn Phe His Ala Ser	Ala Arg Asn Phe His Ala Ser Asn Thr His Leu Gin Lys Thr Gly Thr	n Lys Thr Gly Thr
450	0	455	460		•		8	35	40	45

WO 2004/055519		PCT/EP2003/014057	PACE SOLVE CONTRACTOR OF THE S	
	273/335		274/335	/c0+1
Ala Glu Met	Ala Glu Met Ser Ser Ile Leu Glu Glu Arg Ile Leu Gly	G lle Leu Gly Ala Asp Thr	Lys Leu Tyr Cys Ile Tyr Val Ala Ile Gly Gln Lys Arg Ser Thr Val	
20	55	09	245 250 255	
Ser Val Asp	Ser Val Asp Leu Glu Glu Thr Gly Arg Val Leu Ser Ile	l Leu Ser Ile Gly Asp Gly	Ala Gln Leu Val Lys Arg Leu Thr Asp Ala Asp Ala Met Lys Tyr Thr	
. 59	70	75 80	260 265 270	
5 Ile Ala Arg	Ile Ala Arg Val His Gly Leu Arg Asn Val Gln Ala Glu	l Gin Ala Giu Giu Met Val	5 Ile Val Val Ser Ala Thr Ala Ser Asp Ala Ala Pro Leu Gln Tyr Leu	
	85 90	95	275 280 285	
Glu Phe Ser	Glu Phe Ser Ger Gly Leu Lys Gly Met Ser Leu Asn Leu	f Leu Asn Leu Glu Pro Asp	Ala Pro Tyr Ser Gly Cys Ser Met Gly Glu Tyr Phe Arg Asp Asn Gly	
	100 105	110	290 295 300	
Asn Val Gly	Asn Val Gly Val Val Val Phe Gly Asn Asp Lys Leu Ile	. Lys Leu Ile Lys Glu Gly	Lys His Ala Leu Ile Ile Tyr Asp Asp Leu Ser Lys Gln Ala Val Ala	
10 115	120	125	10 305 310 315 320	
Asp Ile Val	Asp ile Val Lys Arg Thr Gly Ala ile Val Asp Val Pro Val Gly Glu	Asp Val Pro Val Gly Glu	Tyr Arg Gln Met Ser Leu Leu Arg Arg Pro Pro Gly Arg Glu Ala	
130	. 135	140	325 330 335	
Glu Leu Leu	Glu Leu Leu Gly Arg Vel Val Asp Ala Leu Gly Asn Ala Ile Asp Gly	Gly Asn Ala Ile Asp Gly	Tyr Pro Gly Asp Val Phe Tyr Leu His Ser Arg Leu Glu Arg Ala	
145	150	155 160	340 345 . 350	
15 Lys Gly Pro	Lys Gly Pro Ile Gly Ser Lys Thr Arg Arg Arg Val Gly Leu Lys Ala	Arg Val Gly Leu Lys Ala	is Ala Lys Met Asn Asp Ala Phe Gly Gly Gly Ser Leu Thr Ala Leu Pro	
	165 170	175	355 360 365	
Pro Gly 11e	Pro Gly lle Ile Pro Arg ile Ser Val Arg Glu Pro Met Gln Thr Gly	Glu Pro Met Gln Thr Gly	Val ile Glu Thr Gln Ala Gly Asp Val Ser Ala Tyr ile Pro Thr Asn	
	180 185	190	370 375 380	
Ile Lys Ala	Ile Lys Ala Val Asp Ser Leu Val Pro Ile Gly Arg Gly Gln Arg	Oly Arg Gly Gln Arg Glu	Val ile Ser ile Thr Asp Gly Gln ile Phe Leu Glu Thr Glu Leu Phe	
20 195	200	. 205	20 385 390 395 400	
Leu Ile Ile	Leu ile ile Gly Asp Arg Gin Thr Gly Lys Thr Ser ile Ala ile Asp	Thr Ser Ile Ala Ile Asp	Tyr Lys Gly Ile Arg Pro Ala Ile Asn Val Gly Leu Ser Val Ser Arg	
210	. 215	220	405 410. 415	
Thr Ile Ile ;	Thr Ile Ile Asn Gln Lys Arg Phe Asn Asp Gly Ser Asp	Gly Ser Asp Glu Lys Lys	Val Gly Ser Ala Ala Gln Thr Arg Ala Met Lys Gln Val Ala Gly Thr	
225	230	235 240	.420 .425 430	

WO 2004/055519 PCT/EP2003/014057 275/335	WO 2004/055519 PCT/EP2003/014057 276/335
Met Lys Leu Glu Leu Ala Gln Tyr Arg Glu Val Ala Ala Phe Ala Gln	<222> (1)(742)
435 440 445	. <223> Accession No. as of 29 August 2003: P19835
Phe Gly Ser Asp Leu Asp Ala Ala Thr Gln Gln Leu Leu Ser Arg Gly	<400> 91
450 460	
5 Val Arg Leu Thr Glu Leu Leu Lys Gln Gly Gln Tyr Ser Pro Met Ala	5 Met Gly Arg Leu Gln Leu Val Val Leu Gly Leu Thr Cys Cys Trp Ala
465 470 475 480	1 5 10 15
ile Glu Glu Gln Val Ala Val Ile Tyr Ala Gly Val Arg Gly Tyr Leu	. Val Ala Ser Ala Ala Lys Leu Gly Ala Val Tyr Thr Glu Gly Gly Phe
485 490 495	20 25 30
Asp Lys Leu Glu Pro Ser Lys Ile Thr Lys Phe Glu Asn Ala Phe Leu	Val Glu Gly Val Asn Lys Lys Leu Gly Leu Leu Gly Asp Ser Val Asp
10 500 505 510	10 35 40 45
Ser His Val Val Ser Gln His Gln Ala Leu Leu Gly Thr Ile Arg Ala	Ile Phe Lys Gly Ile Pro Phe Ala Ala Pro Thr Lys Ala Leu Glu Asn
515 520 525 .	09 52 05
Asp Gly Lys Ile Ser Glu Gln Ser Asp Ala Lys Leu Lys Glu Ile Val	Pro Gln Pro His Pro Gly Trp Gln Gly Thr Leu Lys Ala Lys Asn Phe
530 535 .	65 70 75 80
15 Thr Asn Phe Leu Ala Gly Phe Glu Ala	15 Lys Lys Arg Cys Leu Gln Ala Thr Ile Thr Gln Asp Ser Thr Tyr Gly
545 550	56 06 . S8 .
	Asp Glu Asp Cys Leu Tyr Leu Asn Ile Trp Val Pro Gln Gly Arg Lys
	100 105 110
<210> 91	Gin Val Ser Arg Asp Leu Pro Val Met Ile Trp Ile Tyr Gly Gly Ala
20 <211> 742	20 115 120 125
-<212> PRT	Phe Leu Met Gly Ser Gly His Gly Ala Asn Phe Leu Asn Asn Tyr Leu
<213> Homo sapiens	130 135 140
<2220>	Tyr Asp Gly Glu Glu Ile Ala Thr Arg Gly Asn Val Ile Val Val Thr

	WO 2004/055519	277/335	PCT/EP2003/014057	-WO 2004/055519 278/335	PCT/EP2003/0:
	Phe Asn Tyr Arg Val Gly Pro Leu Gly Phe Leu Ser Thr Gly Asp Ala	o Leu Gly Phe Leu Ser Thr	Gly Asp Ala	Asn Lys Gly Asn Lys Lys Val Thr Glu Glu Asp Phe Tyr Lys Leu Val	lu Glu Asp Phe Tyr Lys Leu Val
	165	170	175	355 360	365
	Asn Leu Pro Gly Asn Tyr Gly Leu Arg Asp Gln His Met Ala Ile Ala	' Leu Arg Asp Gln His Met .	Ala Ile Ala	Ser Glu Phe Thr Ile Thr Lys Gly Leu Arg Gly Ale Lys Thr Thr Phe	eu Arg Gly Ala Lys Thr Thr Phe
	180	185	190	370 375	380
'n	Trp Val Lys Arg Asn Ile Ala Ala Phe Gly Gly Asp Pro Asn Asn Ile	Ala Phe Gly Gly Asp Pro	Asn Ile 5	Asp Val Tyr Thr Glu Ser Trp Ala Gln Asp Pro Ser Gln Glu Asn Lys	n Asp Pro Ser Gln Glu Asn Lys
	195	200 , 205		385 390	395 400
•	Thr Leu Phe Gly Glu Ser Ala Gly Gly Ala Ser Val Ser Leu Gln Thr	Gly Gly Ala Ser Val Ser I	.eu Gin Thr	Lys Lys Thr Vel Vel Asp Phe Glu Thr Asp Vel Leu Phe Leu Val Pro	ir Asp Val Leu Phe Leu Val Pro
	210 215	. 220		405	410 415
	Leu Ser Pro Tyr Asn Lys Gly Leu Ile Arg Arg Ala Ile Ser Gln Ser	Leu Ile Arg Arg Ala Ile S	er Gln Ser	Thr Glu Ile Ala Leu Ala Gln His Arg Ala Asn Ala Lys Ser Ala Lys	g Ala Asn Ala Lys Ser Ala Lys
9	225 230	235	240 10	420 425	.5 430
	Gly Val Ala Leu Ser Pro Trp Val Ile Gln Lys Asn Pro Leu Phe Trp	Val Ile Gln Lys Asn Pro L	eu Phe Trp	Thr Tyr Ala Tyr Leu Phe Ser His Pro Ser Arg Met Pro Val Tyr Pro	o Ser Arg Met Pro Val Tyr Pro
	245	250	. 255	435 440	. 545
	Ala Lys Lys Val·Ala Glu Lys Val Gly Cys Pro Val Gly Asp Ala Ala	Val Gly Cys Pro Val Gly A	sp Ala Ala	Lys Trp Val Gly Ala Asp His Ala Asp Asp Ile Gln Tyr Val Phe Gly	p Asp Ile Gln Tyr Val Phe Gly
	260	265	270	450 455	. 460
15	Arg Met Ala Gin Cys Leu Lys Val Thr Asp Pro Arg Ala Leu Thr Leu	Val Thr Asp Pro Arg Ala L	eu Thr Leu	Lys Pro Phe Ala Thr Pro Thr Gly Tyr Arg Pro Gln Asp Arg Thr Val	r Arg Pro Gln Amp Arg Thr Val
	275	280 285		465 470	475 480
	Ala Tyr Lys Val Pro Leu Ala Gly Leu Glu Tyr Pro Met Leu His Tyr	Gly Leu Glu Tyr Pro Met L	eu His Tyr	Ser Lys Ala Met Ile Ala Tyr Trp Thr Asn Phe Ala Lys Thr Gly Asp	r Asn Phe Ala Lys Thr Gly Asp
	290 295	300		485	490 495
	Val Gly Phe Val Pro Val Ile Asp Gly Asp Phe Il	Asp Gly Asp Phe Ile Pro A	e Pro Ala Asp Pro	Pro Asn Met Gly Asp Ser Ala Val Pro Thr His Trp Glu Pro Tyr Thr	o Thr His Try Glu Pro Tyr Thr
20	305 310	315	320 20	500 505	5 510
	Ile Asn Leu Tyr Ala Asn Ala Ala Asp Ile Asp Tyr Ile Ala Gly Thr	Ala Asp Ile Asp Tyr Ile Al	ta Gly Thr	Thr Glu Asn Ser Gly Tyr Leu Glu Ile Thr Lys Lys Met Gly Ser Ser	e Thr Lys Lys Met Gly Ser Ser
	325	330	335	515 . 520	525
	Asn Asn Met Asp Gly His Ile Phe Ala Ser Ile Asp Met Pro Ala Ile	Phe Ala Ser Ile Asp Met Pa	o Ala Ile	Ser Met Lys Arg Ser Leu Arg Thr Asn Phe Leu Arg Tyr Trp Thr Leu	n Phe Leu Arg Tyr Try Thr Leu
	340	345 350	01	530 535	540

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PCT/EP2003/014057										in precursor		003: P54315			e Leu Leu Gly Ala Ala Lys	15	/ Cys Phe Ser Asp Thr Glu	30	Lys Ile Leu Pro Trp Ser	45	Tyr Thr Asn Glu Asn Pro		Pro Ser Thr Ile Glu Ala	75 80
WO 2004/055519 280/335	Pro Ala Val Ile Arg Phe	740			5 <210> 92	<211> 467	<212> PRT	<213> Homo sapiens	<220>	10 <221> Pancreatic lipase related protein precursor	<222> (1)(467)	<223> Accession No. as of 29 August 2003; P54315	<400> 92		is Met Leu Ile Phe Trp Thr Ile Thr Leu Phe Leu Leu Gly Ala Ala Lys	1 5 10	Gly Lys Glu Val Cys Tyr Glu Asp Leu Gly Cys Phe Ser Asp Thr Glu	20 25	Pro Trp Gly Gly Thr Ala 11e Arg Pro Leu Lys 11e Leu Pro Trp Ser	20 35 40	Pro Glu Lys Ile Gly Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro	55 . 05	Asn Asn Phe Gln Ile Leu Leu Ser Asp Pro Ser Thr Ile Glu Ala	65 70
WO 2004/055519 PCT/EP2003/014057 279/335	Thr Tyr Leu Ala Leu Pro Thr Val Thr Asp Gln Glu Ala Thr Pro Val	545 550 555 560.	Pro Pro Thr Gly Asp Ser Glu Ala Thr Pro Val Pro Pro Thr Gly Asp	565 570 575	5 Ser Glu Thr Ala Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro	586 585 590	Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly	595 600 865	Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro	10 610 615 620	Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr	625 630 635 640	Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly Ala	645 650 655	15 Pro Pro Val Pro Pro Thr Gly Asp Ala Gly Pro Pro Pro Val Pro Pro	660 665 670	Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly	675 680 685	Ala Pro Pro Val Thr Pro Thr Gly Asp Ser Glu Thr Ala Pro Val Pro	20 690 695 700	Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser	705 710 715 720	Glu Ala Ala Pro Val Pro Pro Thr Asp Asp Ser Lys Glu Ala Gln Met	725 730 735

WO 2004/055519 PCT/EP2003/014057 281/335	WO 2004/055519 PCT/EP2003/01 282/335
Ser Asn Phe Gin Met Asp Arg Lys Thr Arg Phe 11e 11e His Gly Phe	Thr Arg Asp Phe Val Ala Cys Asn His Leu Arg Ser Tyr Lys Tyr Tyr
85 90 95	275 280 285
ile Asp Lys Gly Asp Glu Ser Trp Val Thr Asp Met Cys Lys Lys Leu	Leu Glu Ser Ile Leu Asn Pro Asp Gly Phe Ala Ayr Pro Cys Thr
100 105 110	. 300 . 300 .
? Phe Glu Val Glu Val Asn Cys Ile Cys Val Asp Trp Lys Lys Gly	5 Ser Tyr Lys Ser Phe Glu Ser Asp Lys Cys Pro Cys Pro Asp Gln
115 120 125	305 310 315 320
Ser Gin Ala Thr Tyr Thr Gin Ala Ala Asn Asn Val Arg Val Val Gly	Gly Cys Pro Gln Met Gly His Tyr Ala Asp Lys Phe Ala Gly Arg Thr
130 135 140	325 330 335
Ala Gln Vel Ala Gln Met Leu Asp Ile Leu Ieu Thr Glu Tyr Ser Tyr	Ser Glu Glu Gln Iys Phe Phe Leu Asn Thr Gly Glu Ale Ser Asn
) 145· 150 155 160	10 340 345 350
Pro Pro Ser Lys Val His Leu Ile Gly His Ser Leu Gly Ala His Val	Phe Ala Arg Trp Arg Tyr Gly Val Ser 11e Thr Leu Ser Gly Arg Thr
165 170 175	355 360 355
Ala Gly Glu Ala Gly Ser Lys Thr Pro Gly Leu Ser Arg Ile Thr Gly	Ala Thr Gly Gln Ile Lys Val Ala Leu Phe Gly Asn Lys Gly Asn Thr
180 185 190	370
Leu Asp Pro Val Glu Ala Ser Phe Glu Ser Thr Pro Glu Glu Val Arg	15 His Gin Tyr Ser ile Phe Arg Gly ile Leu Lys Pro Gly Ser Thr His
195 200 205	385 390 395 400
Leu Asp Pro Ser Asp Ala Asp Phe Val Asp Val Ile His Thr Asp Ala	Ser Tyr Glu Phe Asp Ala Lys Leu Asp Val Gly Thr Ile Glu Lys Val
210 215 220	405 410 415
Ala Pro Leu Ile Pro Phe Leu Gly Phe Gly Thr Asn Gln Gln Met Gly	Lys Phe Leu Trp Asn Asn Asn Val Ile Asn Pro Thr Leu Pro Lys Val
225 230 235 240	20 420 425 430
His Leu Asp Phe Pro Asn Gly Gly Glu Ser Met Pro Gly Cys Lys	Gly Ale Thr Lys Ile Thr Val Gln Lys Glu Glu Lys Thr Val Tyr
245 250 255	435 440 445
Lys Asn Ala Leu Ser Gin Ile Val Asp Leu Asp Gly Ile Trp Ala Gly	Asn Phe Cys Ser Glu Asp Thr Val Arg Glu Asp Thr Leu Leu Thr Leu
260 265 270	450 . 455 460

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WO 2004/055519 PCT/EP2003/014057 284/335	Ser Asn Phe Gln Leu Asp Arg Lys Thr Arg Phe Ile 11e His Gly Phe	56 06 58	Leu Asp Lys Ala Glu Asp Ser Trp Pro Ser Asp Met Cys Lys Lys Met	100 105 110	5 Phe Glu Val Glu Lys Val Asn Cys Ile Cys Val Asp Trp Arg His Gly	115 120	Ser Arg Ala Met Tyr Thr Gln Ala Val Gln Asn Ile Arg Val Val Gly	130 135 140	Ala Glu Thr Ala Phe Leu Ile Gln Ala Leu Ser Thr Gln Leu Gly Tyr	10 145 150 155 160	Ser Leu Glu Asp Val His Val Ile Gly His Ser Leu Gly Ala His Thr	165 170 175	Ala Ala Glu Ala Gly Arg Arg Leu Gly Gly Arg Val Gly Arg Ile Thr	180 185 190	15 Gly Leu Asp Pro Ala Gly Pro Cys Phe Gln Asp Glu Pro Glu Glu Val	1.95 200 205	Arg Leu Asp Pro Ser Asp Ala Val Phe Val Asp Vel Ile His Thr Asp	210 215 220	Ser Ser Pro 11e Val Pro Ser Leu Gly Phe Gly Met Ser Gln Lys Val	20 225 230 235 240	Gly His Leu Asp Phe Pro Asn Gly Gly Lys Glu Met Pro Gly Cys	. 245 250 255	Lys Lys Asn Val Leu Ser Thr Ile Thr Asp Ile Asp Gly Ile Trp Glu	260 265 270
WO 2004/055519 PCT/EP2003/014057 283/335	Thr Pro Cys	465			5 <210> 93	<211> 469	<212> PRT	<213> Homo sapiens	<220>	10 <221> Pancreatic lipase related protein 2 procursor	<222> (1)(469)	<223> Accession No. as of 29 August 2003; P54317	<400> 93		15 Met Leu Pro Pro Trp Thr Leu Gly Leu Leu Leu Ala Thr Val Arg	1 5 10 . 15	Gly Lys Glu Val Cys Tyr Gly Gln Leu Gly Cys Phe Ser Asp Glu Lys	. 20 25 30	Pro Trp Ala Gly Thr Leu Gln Arg Pro Val Lys Leu Leu Pro Trp Ser	20 35 40 . 45	Pro Glu Asp Ile Asp Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro		Asn Asn Phe Gln Leu Ile Thr Gly Thr Glu Pro Asp Thr Ile Glu Ala	65 70 75 80

	WO 2004/055519	PCT/EP2003/014057	WO 2004/055519	03/01/067
	285/335		286/335	
	Gly Ile Gly Gly Phe Val Ser Cys Asn His Leu Arg Ser P	Phe Glu Tyr	Ser Leu Tyr Pro Cys	
	275 280 285		465	
	Tyr Ser Ser Val Leu Asn Pro Asp Gly Phe Leu Gly Ty	Tyr Pro Cys		
	290 . 295 300			
	5 Ala Ser Tyr Asp Glu Phe Gln Glu Ser Lys Cys Phe Pro C	Cys Pro Ala 5	5 <210> 94	
	305. 310 315	320	<211> 465	
	Glu Gly Cys Pro Lys Met Gly His Tyr Ala Asp Gln Phe Ly	Lys Gly Lys	<212> PRT	
	325 330	. 335	<213> Homo sapiens	
	Thr Ser Ala Vel Glu Gln Thr Phe Phe Leu Aen Thr Gly Gl	Glu Ser Gly	<220>	
ā	10 340 345 35	350 . 10	<221> Triacylglycerol lipase, pancreatic precursor	
	Asn Phe Thr Ser Trp Arg Tyr Lys Val Ser Val Thr Leu Se	Ser Gly Lys	<222> (1)(465)	
	355 360 365		<223> Accession No. as of 29 August 2003; P16233	
	Glu Lys Val Asn Gly Tyr Ile Arg Ile Ala Leu Tyr Gly Se	Ser Asn Glu	<400> 94	
	370 375 380		,	
15	Asn Ser Lys Gln Tyr Glu Ile Phe Lys Gly Ser Leu Lys	Pro Asp Ala	Met Leu Pro Leu Trp Thr Leu Ser Leu Leu Leu Gly Ala Val Ala Gly	
	395 390 395	400	1 5 10 15	
	Ser His Thr Cys Ala Ile Asp Val Asp Phe Asn Val Gly Lys Ile Gln	s ile Gin	Lys Glu Val Cys Tyr Glu Arg Leu Gly Cys Phe Ser Asp Asp Ser Pro	
	405 410	415	20 . 25 30	
	Lys Val Lys Phe Leu Trp Asn Lys Arg Gly 11e Asn Leu Ser Glu Pro	r Glu Pro	Trp Ser Gly Ile Thr Glu Arg Pro Leu His Ile Leu Pro Trp Ser Pro	
20	420 425 430	0 20	35 40 45	
	Lys Leu Gly Ala Ser Gln Ile Thr Val Gln Ser Gly Glu Asp Gly Thr	p Gly Thr	Lys Asp Val Asn Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro Asn	
	435 440 445		50 55 60	
	Glu Tyr Asn Phe Cys Ser Ser Asp Thr Val Glu Glu Asn Val Leu Gln	l Leu Gln	Asn Phe Gln Glu Val Ala Ala Asp Ser Ser Ser Ile Ser Gly Ser Asn	
	450 455 460		65 70 75 80	

WO 2004/055519	PCT/EP2003/014057	WO 2004/053519 PCT/EP2003/01
	287/335	288/335
Phe Lys Thr Asn Arg	Phe Lys Thr Asn Arg Lys Thr Arg Phe Ile Ile His Gly Phe Ile Asp	Arg Asp Phe Ala Ala Cys Asn His Leu Arg Ser Tyr Lys Tyr Thr
85	56 06 .	275 280 285
Lys Gly Glu Glu Asn	Lys Gly Glu Glu Asn Trp Leu Ala Asn Val Cys Lys Asn Leu Phe Lys	Asp Ser Ile Val Asn Pro Asp Gly Phe Ala Gly Phe Pro Cys Ala Ser
100	105 110	290 295 300
5 Val Glu Ser Val Asn	Val Glu Ser Val Asn Cys Ile Cys Val Asp Trp Lys Gly Gly Ser Arg	5 Tyr Asn Val Phe Thr Ala Asn Lys Cys Pro Cys Pro Ser Gly Gly
115	120 . 125	305 310 315 320
Thr Gly Tyr Thr Gln	Thr Gly Tyr Thr Gln Ala Ser Gln Asn Ile Arg Ile Val Gly Ala Glu	Cys Pro Gln Met Gly His Tyr Als Asp Arg Tyr Pro Gly Lys Thr Asn
130	135 140	325 330 335
Val Ala Tyr Phe Val	Val Ala Tyr Phe Val Glu Phe Leu Gln Ser Ala Phe Gly Tyr Ser Pro	Asp Val Gly Gln Lys Phe Tyr Leu Asp Thr Gly Asp Ala Ser Asn Phe
10 145	150 155 160	. 10 340 345 350
Ser Asn Val His Val	Ser Asn Val His Val Ile Gly His Ser Leu Gly Ala His Ala Ala Gly	Ala Arg Trp Arg Tyr Lys Val Ser Val Thr Leu Ser Gly Lys Val
. 165	. 170 175	355 360 365
Glu Ala Gly Arg Arg	Glu Ala Gly Arg Arg Thr Asn Gly Thr Ile Gly Arg Ile Thr Gly Leu	Thr Gly His Ile Leu Val Ser Leu Phe Gly Asn Lys Gly Asn Ser Lys
180	185 190	370 375 380
15 Asp Pro Ala Glu Pro	Asp Pro Ala Glu Pro Cys Phe Gln Gly Thr Pro Glu Leu Val Arg Leu	15 Gln Tyr Glu 11e Phe Lys Gly Thr Leu Lys Pro Asp Ser Thr His Ser
195	200 205	385 390 395 400
Asp Pro Ser Asp Ala	Asp Pro Ser Asp Ala Lys Phe Val Asp Val Ile His Thr Asp Gly Ala	Asn Glu Phe Asp Ser Asp Vel Asp Val Gly Asp Leu Gln Met Val Lys
210	215 220	405 410 415
Pro Ile Val Pro Asn	Pro Ile Val Pro Asn Leu Gly Phe Gly Met Ser Gln Val Val Gly His	Phe Ile Trp Tyr Asn Asn Val Ile Asn Pro Thr Leu Pro Arg Val Gly
20 225	230 235 240	20 420 425 430
Leu Asp Phe Phe Pro	Leu Asp Phe Phe Pro Asn Gly Gly Val Glu Met Pro Gly Cys Lys Lys	Ala Ser Lys Ile Ile Val Glu Thr Asn Val Gly Lys Gln Phe Asn Phe
. 245	250 255	435 440 445
Asn Ile Leu Ser Gln	Asn ile Leu Ser Gln ile Val Asp ile Asp Gly ile Trp Glu Gly Thr	Cys Ser Pro Glu Thr Val Arg Glu Glu Val Leu Leu Thr Leu Thr Pro
260	265 270	450 . 455 . 460

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.WO 2004/055519	289/335	PCT/EP2003/014057	WO 2004/055519 290/335	PCT/EP2003/014057
Сув			Gln Gly Met Thr Ser Ala Asp Asp Phe Phe Gln Gly Thr Lys Ala Ala	r Lys Ala Ala
465			06 58	56
			Leu Ala Gly Gly Thr Thr Met Ile Ile Asp His Val Val Pro Glu Pro	l Pro Glu Pro
			100 . 105	110
5 <210> 95			5 Gly Thr Ser Leu Leu Ala Ala Phe Asp Gln Trp Arg Glu Trp Ala Asp	1 Trp Ala Asp
<211> 572			115 120 125	
<212> PRT			Ser Lys Ser Cys Cys Asp Tyr Ser Leu His Val Asp Ile Ser Glu Trp	s Ser Glu Trp
<213> Homo sapiens			130 135 140	
<220>			His Lys Gly Ile Gln Glu Glu Met Glu Ala Leu Val Lys Asp His Gly	Asp His Gly
10 <221> Dihydropyrimidinase related protein-2	e related protein-2	٠.	10 145 150 155	160
<222> (1)(572)			Val Asn Ser Phe Leu Val Tyr Met Ala Phe Lys Asp Arg Phe Gln Leu	r Phe Gln Leu
<223> Accession No. as o	Accession No. as of 29 August 2003: Q16555		165 170	175
<400> 95			Thr Asp Cys Gln Ile Tyr Glu Val Leu Ser Val Ile Arg Asp Ile Gly	Asp Ile Gly
				190
15 Met Ser Tyr Gln Gly Lys L	Met Ser Tyr Gin Gly Lys Lys Asn ile Pro Arg ile Thr Ser Asp Arg	er Asp Arg	is Ala Ile Ala Gln Val His Ala Glu Asn Gly Asp Ile Ile Ala Glu Glu	Ala Glu Glu
1 5	10	15	195 200 205	
Leu Leu Ile Lys Gly Gly L	Leu Leu Ile Lys Gly Gly Lys Ile Val Asn Asp Asp Gln Ser Phe Tyr	er Phe Tyr	Gin Gin Arg Ile Leu Asp Leu Gly Ile Thr Gly Pro Glu Gly His Val	Gly His Val
. 50	25	30	. 210 215 220	
Ala Asp Ile Tyr Met Glu A	Ala Asp ile Tyr Met Glu Asp Gly Leu ile Lys Gln ile Gly Glu Asn	ly Glu Asn	Leu Ser Arg Pro Glu Glu Val Glu Ala Glu Ala Val Asn Arg Ala Ile	Arg Ala Ile
35	40 45		20 225 230 235	240
Leu Ile Val Pro Gly Gly V.	Leu lle Val Pro Gly Gly Val Lys Thr lle Glu Ala His Ser Arg Met	er Arg Met	Thr Ile Ala Asn Gln Thr Asn Cys Pro Leu Tyr Ile Thr Lys Val Met	Lys Val Met
50 55	09		245 . 250	255
Val lle Pro Gly Gly Ile Au	Val 11e Pro Gly Gly 11e Asp Val His Thr Arg Phe Gln Met Pro Asp	et Pro Asp	Ser Lys Ser Ser Ala Glu Val Ile Ala Gln Ala Arg Lys Lys Gly Thr	Lys Gly Thr
65 70	7.5	08	260 265	270

450 . 455 . 460
Gln Gly Lys Ile Val Leu Glu Asp Gly Thr Leu His Val Thr Glu Gly
. 435 440 445
Ile Phe Glu Gly Met Glu Cys Arg Gly Ser Pro Leu Val Val Ile Ser
20 420 425 430
Val Lys Thr Ile Ser Ala Lys Thr His Asn Ser Ser Leu Glu Tyr Asn
. 405 410 415
ile Ala Val Gly Ser Asp Ala Asp Leu Val Ile Trp Asp Pro Asp Ser
385 390 395 400
15 Ser Thr Asn Ala Ala Lys Val Phe Asn Leu Tyr Pro Arg Lys Gly Arg
370 375 380
Ala Val Val Thr Gly Lys Met Asp Glu Asn Gln Phe Val Ala Val Thr
355 360 365
Glu Gly Thr Asn Gly Thr Glu Glu Arg Met Ser Val Ile Trp Asp Lys
10 340 345 350
Asn Thr Ala Gln Lys Ala Val Gly Lys Asp Asn Phe Thr Leu Ile Pro
325 330 335
Leu Ser Cys Gly Asp Leu Gln Val Thr Gly Ser Ala His Cys Thr Phe
305 310 315 320
5 Pro Pro Leu Ser Pro Asp Pro Thr Thr Pro Asp Phe Leu Asn Ser Leu
290 295 300
His Tyr Trp Ser Lys Asn Trp Ala Lys Ala Ala Ala Phe Val Thr Ser
275 280 285
Val Val Tyr Gly Glu Pro Ile Thr Ala Ser Leu Gly Thr Amp Gly Ser
WO 2004/055519 . PCT/EP2003/014057

WO 2004/655519	293/335	PCT/EP2003/014057	WO 2004/055519 . 294/335	PCT/EP2003/01
<400> 96	•		Met Trp Tyr Arg Ser Lys Glu Arg Gly Gln Arg Gly Phe Ser Lys Glu	Phe Ser Lys Glu
			180 185	190
Met Ala Ser Met Leu Leu Ala Gin Arg Leu Ala Cys Ser Phe Gin His	Gln Arg Leu Ala Cys Ser 1	Phe Gin His	Glu Leu Glu Thr Cys Met Ile Asn Gln Ala Pro Trp Cys Pro Asp Tyr	Cys Pro Asp Tyr
1 5	10	15	195 200	
5 Thr Tyr Arg Leu Leu Val Pro Gly Ser Arg His Ile Ser Gln Ala Ala	Gly Ser Arg His Ile Ser C	Jin Ala Ala	5 Ser Ile Leu Ser Phe Met Gly Ser Phe His Gly Arg Thr Met Gly Cys	Thr Met Gly Cya
20	25	30	210 215 220	
Ala Lys Val Asp Val Glu Phe Asp Tyr Asp Gly Pro Leu Met Lys	Asp Tyr Asp Gly Pro Leu R	et Lys Thr	Leu Ala Thr Thr His Ser Lys Ala 11e His Lys 11e Asp 11e Pro Ser	Asp Ile Pro Ser
. 35	40 45		225 230 235	240
Glu Val Pro Gly Pro Arg Ser Gln Glu Leu Met Lys Gln Leu Asn Ile	Gln Glu beu Met Lys Gln L	eu Asn Ile	Phe Asp Try Pro Ile Ala Pro Phe Pro Arg Leu Lys Tyr Pro Leu Glu	Tyr Pro Leu Glu
10 50 55	09		10 . 245 . 250	255
Ile Gln Asn Ala Glu Ala Val His Phe Phe Cys Asn Tyr Glu Glu Ser	His Phe Phe Cys Asn Tyr G	ilu Glu Ser	Glu Phe Val Lys Glu Asn Gln Gln Glu Glu Ala Gly Cys Leu Glu Glu	Cys Leu Glu Glu
65 70	. 22	08	260 265 •	270
Arg Gly Asn Tyr Leu Val Asp Val Asp Gly Asn Arg Met Leu Asp Leu	Val Asp Gly Asn Arg Met L	eu Asp Leu	. Val Glu Asp Leu Ile Val Lys Tyr Arg Lys Lys Lys Lys Thr Val Ale	Lys Thr Val Ala
85	06		275 280 2	
15 Tyr Ser Gin Ile Ser Ser Val Pro Ile Gly Tyr Ser Asp Pro Ala Leu	Pro Ile Gly Tyr Ser Asp P	ro Ala Leu	15 Gly Ile Ile Val Glu Pro Ile Gln Ser Glu Gly Gly Asp Asn His Ale	Asp Asn His Ale
100	105	110	290 295 300	
Val Lys Leu Ile Gln Gln Pro Gln Asn Ala Ser Met Phe Val Asn Arg	in Asn Ala Ser Met Phe Vi	al Asn Arg	Ser Asp Asp Phe Phe Arg Lys Leu Arg Asp Ile Ala Arg Lys His Cys	Arg Lys His Cys
. 115 1	120 125		305 310 315	320
Pro Ala Leu Glu Ile Leu Pro Pro Glu Asn Phe Val Glu Lys Leu Arg	ro Glu Asn Phe Val Glu Ly	/s Leu Arg	Cys Ala Phe Leu Val Asp Glu Val Gln Thr Gly Gly Gly Cys Thr Gly	Gly Cys Thr Gly
20 130 135	140		325 330	335
Gln Ser Leu Leu Ser Val Ala Pro Lys Gly Met Ser Gln Leu Ile Thr	ro Lys Gly Met Ser Gln Le	su lle Thr	Lys Phe Try Ala His Glu His Try Gly Leu Asp Asp Pro Ala Asp Val	Pro Ala Asp Val
145	155		340 345	350
Met Ala Cys Gly Ser Cys Ser Asn Glu Asn Ala Leu Lys Thr Ile Phe	sn Glu Asn Ala Leu Lys Th	ır Ile Phe	Met Thr Phe Sex Lys Lys Met Met Thr Gly Gly Phe Phe Leu Lys Glu	Phe Leu Lys Glu
165	170	175	355	365

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WO 2004/055519 PCT/EP7003/014057	WO 2004/055519 PCT/EP2003/01405
295/335	296/335
Glu Phe Arg Pro Asn Ala Pro Tyr Arg Ile Phe Asn Thr Trp Leu Gly	<220>
376 . 375 . 380	<221> Glycine amidiontransferase, mitochondrial precursor
Asp Pro Ser Lys Asn Leu Leu Leu Ala Glu Val lle Asn Ile 11e Lys	<222> (1)(423)
385 390 395 400	<223> Acceston No. as of 29 August 2003; P50440
5 Arg Glu Asp Leu Leu Asn Asn Ala Ala His Ala Gly Lys Ala Leu Leu	5 <400> 97
405 410 415	
Thr Gly Leu Leu Asp Leu Gln Ala Arg Tyr Pro Gln Phe Ile Ser Arg	Met Leu Arg Val Arg Cys Leu Arg Gly Gly Ser Arg Gly Ala Glu Ala
420 425 430	1 5 10 15
Val Arg Gly Arg Gly Thr Phe Cys Ser Phe Asp Thr Pro Asp Asp Ser	. Val His Tyz Ile Gly Ser Arg Leu Gly Arg Thr Leu Thr Gly Trp Val
10 435 440 445	10 20 25 30
Ile Arg Asn Lys Leu Ile Leu Ile Ala Arg Asn Lys Gly Val Val Leu	Gln Arg Thr Phe Gln Ser Thr Gln Ala Ala Thr Ala Ser Ser Arg Asn
450 455 460	35 40 45
Gly Gly Cys Gly Asp Lys Ser Ile Arg Phe Arg Pro Thr Leu Val Phe	Ser Cys Ale Ale Asp Asp Lys Ale Thr Glu Pro Leu Pro Lys Asp Cys
465 470 475 480	. 09 55 05
15 Arg Asp His His Ala His Leu Phe Leu Asn Ile Phe Ser Asp Ile Leu	15 Pro Val Ser Ser Tyr Aen Glu Trp Aep Pro Leu Glu Glu Val Ile Val
485 490 495	65 70 75 80
Ala Asp Phe Lys	Gly Arg Ala Glu Asn Ala Cys Val Pro Pro Phe Thr Ile Glu Val Lys
	56 06 58
	Ala Asn Thr Tyr Glu Lys Tyr Trp Pro Phe Tyr Gln Lys Gln Gly Gly
20	20 100 105 110
<21.0> 97 ·	His Tyr Phe Pro Lys Asp His Leu Lys Lys Ala Val Ala Glu Ile Glu
<211> 423	. 115 120 125
<212> PRT	Glu Met Cys Asn Ile Leu Lys Thr Glu Gly Val Thr Val Arg Arg Pro
<213> Homo sapiens	130 135 140

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1355	298/335
Asp Pro Ile Asp Trp Ser Leu Lys Tyr Lys Thr Pro Asp Phe Glu Ser	ile ile Thr Pro Pro Thr Pro ile ile Pro Asp Asp His Pro Leu Trp
145 150 155 160	340 345 350
Thr Gly Leu Tyr Ser Ala Met Pro Arg Asp lle Leu Ile Val Val Gly	Met Ser Ser Lya Trp Leu Ser Met Asn Val Leu Met Leu Asp Glu Lys
165 170 175	. 355 . 360 365
5 Asn Glu Ile Ile Glu Ala Pro Met Ala Trp Arg Ser Arg Phe Phe Glu	5 Arg Val Met Val Amp Ala Amn Glu Val Pro Ile Gln Lym Met Phe Glu
180 185 . 190	370 375 380
Tyr Arg Ala Tyr Arg Ser Ile Ile Lys Asp Tyr Phe His Arg Gly Ala	Lys Leu Gly Ile Thr Thr Ile Lys Val Asn Ile Arg Asn Ala Asn Ser
195 200 205	385 390 395 400
Lys Trp Thr Thr Ala Pro Lys Pro Thr Met Ala Asp Glu Leu Tyr Asn	Leu Gly Gly Gly Phe His Cys Trp Thr Cys Asp Val Arg Arg Arg Gly
210 215 220	10 405 410 415
Gln Asp Tyr Pro Ile His Ser Val Glu Asp Arg His Lys Leu Ala Ala	Thr Leu Gln Ser Tyr Leu Asp
225 230 235 240	420
Gln Gly Lys Phe Val Thr Thr Glu Phe Glu Pro Cys Phe Asp Ala Ala	
245 250 255	
Asp Phe lie Arg Ala Gly Arg Asp lle Phe Ala Gln Arg Ser Gln Val	15 <210> 98
260 265 270	<211> 654
Thr Asn Tyr Leu Gly Ile Glu Trp Met Arg Arg His Leu Ala Pro Asp	<212> PKT
275 280 285	. <213> Homo sapiens
Tyr Arg Val His Ile Ile Ser Phe Lys Asp Pro Asn Pro Met His Ile	<220>
290 295 300	20 <221> GRP 78
Asp Ala Thr Phe Asn Ile Ile Gly Pro Gly Ile Val Leu Ser Asn Pro	<222> (1)(654)
305 310 315 320	<223> Accession No. as of 29 August 2003; P11021
Asp Axg Pro Cys His Gln Ile Asp Leu Phe Lys Lys Ala Gly Trp Thr	<220>
325 330 335	<221> misc_feature

WO 2004/055519 PCT/EP2003/014057	WO 2004/055519 PCT/EP2003/014057
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<222> (302)(302)	Phe Thr Pro Glu Gly Glu Cys Leu Ile Gly Asp Ala Ala Lys Asn Gln
<223> Xaa can be any naturally occurring amino acid	65 70 75 80
<220>	Leu Thr Ser Asn Pro Lys Asn Thr Val Phe Asp Ala Lys Arg Leu Ile
<221> misc_feature	56 06 58
5 <222> (329)(329)	5 Gly Arg Trp His Asp Pro Ser Val Gln Gln Asp Ile Glu Phe Leu
<223> Xaa can be any naturally occurring amino acid	100 105 110
<220>	Pro Phe Lys Val Val Glu Lys Asn Thr Lys Ser Tyr 11e Gln 11e Asp
<221> misc_feature	115 120 125
<222> (344)(344)	Val Gly Gly Gln Thr Lys Thr Phe Ala Pro Lys Glu Ile Ser Ala
10 <223> Xaa can be any naturally occurring amino acid	10 130 135 140
<220>	Met Val Leu Thr Lys Met Lys Glu Asn Ala Glu Ala Tyr Leu Gly Lys
<221> misc_feature	145 150 155 160
<222> (461)(461)	Val Thr His Ala Val Val Thr Ala Pro Ala Tyr Phe Asn Asp Ala Gln
<223> Xee can be any naturally occurring emino acid	165 170 . 175
15 <400> 98	15 Cys Gln Ala Thr Lys Asp Ala Gly Thr Ile Ala Asp Leu Asn Vel Met
	180 185 190
Met Lys Leu Ser Leu Val Ala Ala Met Leu Leu Leu Leu Ser Ala	Arg Ile Ile Asn Lys Pro Thr Ala Ala Ala Ile Ala Tyr Gly Leu Asp
1 5 10 15	195 200 205
Ala Arg Ala Lys Glu Glu Asp Met Gly Thr Val Val Ala Ile His Leu	Lys Arg Glu Gly Glu Lys Asn Ile Leu Val Phe Asp Leu Gly Gly Gly
20 20 25 30	20 210 215 220
Gly Thr Thr Tyr Pro Cys Val Gly Val Phe Lys Asn Gly Arg Met Glu	Thr Phe Amp Val Ser Leu Leu Thr Ile Amp Amn Gly Vel Phe Lym Val
35 40 45	225 230 235 240
ile ile Ala Asn Asp Gln Gly Asn Arg ile Met Pro Ser Tyr Val Ala	Val Ala Thr Asn Gly Asp Thr Tyr Leu Gly Gly Glu Asp Phe Asp Gln
	245 250 255

WO 2004/055519	301/335	PCT/EP2003/014057	WO 2004/055519	302/335
Arg Val Met Glu His Phe Ile Lys Leu Tyr Lys Lys Lys		Thr Gly Lys	Ser Gln Ile Phe Ser Thr A	Ser Gln Ile Phe Ser Thr Ala Phe Asp Asn Gln Pro Xaa Thr Ile Lys
260	265	270	450	455 460
Asp Val Arg Lys Asp Asn Arg Ala Val Gln Lys Leu Trp		Arg Lys Val	Val Tyr Glu Gly Lys Gln P.	Val Tyr Glu Gly Lys Gln Pro Leu Thr Lys Asp Asn His Leu Leu Gly
275	280 285		465 470	475 . 480
5 Glu Lys Ala Lys Arg Ala Leu Ser Ser Gln His Gln Ala		Xaa Val Ile	5 Thr Phe Asp Leu Thr Gly I	Thr Phe Asp Leu Thr Gly Ile Pro Pro Ala Pro Cys Gly Val Pro Gln
290 295	300		. 485	490.
Glu Ile Glu Ser Phe Tyr Glu Gly Glu Asp Phe Ser	u Gly Glu Asp Phe Ser Glu	Glu Thr Leu Thr	Ile Glu Val Thr Phe Glu Me	ile Glu Val Thr Phe Glu Met Asp Val Ser Asp ile Leu Gln Val Thr
305 310	315	320 .	500	505
Gin Ala Lys Phe Glu Glu Leu Asn Xaa Asp Leu Phe Gin S	u Asn Xaa Asp Leu Phe Gln S	ser Thr Met	Ala Lys Asp Lys Gly Thr Ar	Ala Lys Asp Lys Gly Thr Arg Tyr Lys Asn Lys Ile Thr Ile Thr Asn
325	330	335	10 515	520 . 525
Lys Pro Ser Gln Arg Ser Val Xaa Lys Val Leu Glu Asp S	1 Xaa Lys Val Leu Glu Asp S	er Asp Leu	Asp Gln Asn His Leu Thr Pr	Asp Gln Asn His Leu Thr Pro Glu Asp Ile Glu Arg Met Val Asn Asp
340	345	350	530 535	5 540
Lys Lys Ser Asp Ile Asp Glu Thr Val Leu Val Gly Gly Phe Thr Gln	u Thr Val Leu Val Gly Gly P	he Thr Gln	Ala Glu Lys Phe Ala Glu Gl	Ala Glu Lys Phe Ala Glu Glu Asp Lys Lys Leu Lys Glu Cys Thr Asp
355	360 365		545 550	. 098 288
is lie Pro Lys lie Gin Gin Leu Val Lys Glu Phe Phe Asn Gly Lys Glu	ı Val Lys Glu Phe Phe Asn G		15 Thr Arg Asn Glu Leu Glu Se	Thr Arg Asn Glu Leu Glu Ser Tyr Ala Tyr Ser Leu Lys Asn Gln Ile
370 375	380		398	570 575
Leu Ser Arg Gly Ile Ser Pro Tyr Glu Ala Val Ala Tyr	Tyr Glu Ala Val Ala Tyr G	Gly Ala Ala	Gly Asp Lys Glu Lys Leu Gl	Gly Asp Lys Glu Lys Leu Gly Gly Lys Leu Ser Glu Asp Lys Glu
385 390	395	007	280	585
Val Gin Ala Gly Val Leu Ser Gly Asp Gin Asp Thr Gly Asp Leu Val	: Gly Asp Gln Asp Thr Gly A	gp Leu Val	Thr Met Glu Lys Thr Val Glu	Thr Met Glu Lys Thr Val Glu Glu Lys Thr Glu Trp Leu Glu Ser His
405	410	415		. 509 009
Leu Leu Asp Ile Cys Pro Leu Thr Leu Gly Ile Glu Thr Val Gly Gly	Thr Leu Gly Ile Glu Thr V	al Gly Gly	Gin Asp Ala Asp Thr Glu Asr	Gin Asp Ala Asp Thr Glu Asp Phe Lys Ala Lys Lys Lys Glu Leu Glu
. 420	425 42	430	. 610 615	620
Val Met Thr Lys Leu Ile Pro Arg Asn Thr Val Val Pro Thr Lys Lys	Arg Asn Thr Val Val Pro I	и гув гув	Glu Ile Val Gin Pro Ile Ile	Glu ile Val Gin Pro ile ile Ser Lys Leu Tyr Gly Ser Ala Gly Pro
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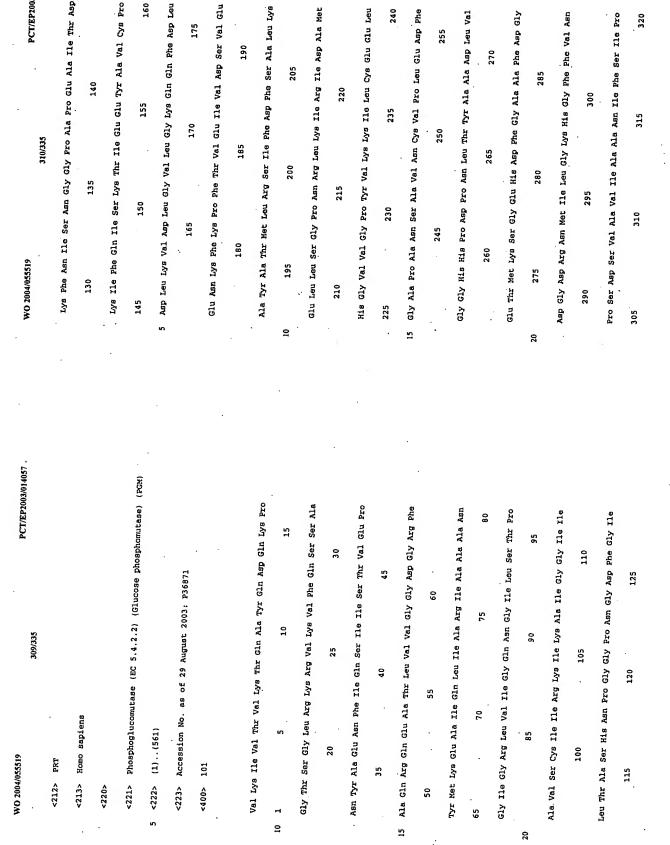
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. 10	15	200 205	
Lys Tyr Asn Arg Glu Gly Asp Leu Leu Phe Thr Val Ala L	Ala Lys Asp Pro	Asp Asn Thr Ala Lys Leu Phe Asp Ser Thr Thr Leu Glu His Gln Lys	Gln Lys
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ile Val Asn Val Trp Tyr Ser Val Asn Gly Glu Arg Leu Gl	Leu Gly Thr Tyr	Thr Phe Arg Thr Glu Arg Pro Val Asn Ser Ala Ala Leu Ser Pro Asn	. Pro Asn
20 35 40 45	20	225 230 235	240
Met Gly His Thr Gly Ala Val Trp Cys Val Asp Ala Asp Tr	Asp Trp Asp Thr	Tyr Asp His Val Val Leu Gly Gly Gly Glu Ala Met Asp Val Thr	Val Thr
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Lys His Val Leu Thr Gly Ser Ala Asp Asn Ser Cys Arg Le	Arg Leu Trp Asp	Thr Thr Ser Thr Arg Ile Gly Lys Phe Glu Ala Arg Phe Phe His Leu	His Leu
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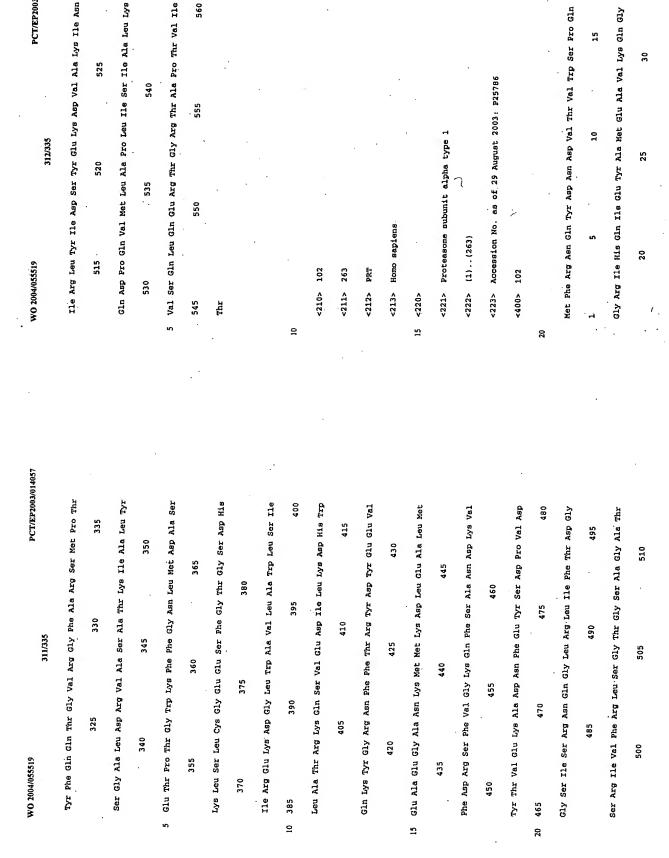
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Asn Ser Val Ala Phe His Pro As	Asn Ser Val Ala Phe His Pro Asp Gly Lys Ser Tyr Ser Gly Gly	Leu ile Val Pro Gly Gly Val Lys Thr ile Glu Ala His Ser Arg Met
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Leu Leu lle Lys Gly Gly Lys lle Val Asn Asp Asp	Val Asn Asp Asp Gln Ser Phe Tyr	Gln Gln Arg Ile Leu Asp Leu Gly Ile Thr Gly Pro Glu Gly His Val
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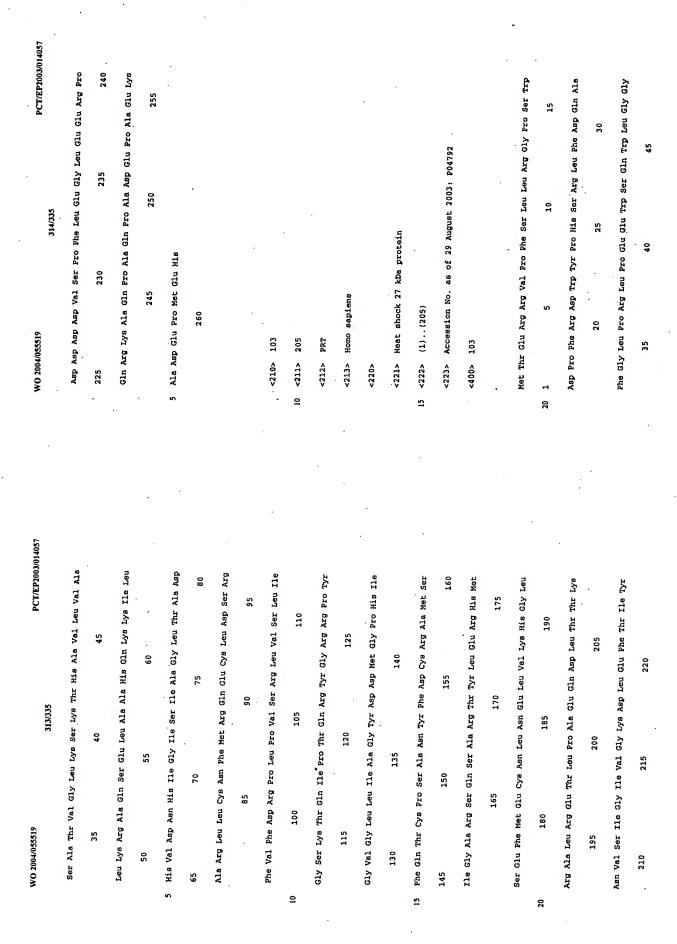
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	Thr ile Ala Asn Gln Thr Asn Cys Pro Leu Tyr Ile Thr Lys Val Met	Ile Phe Glu Gly Met Glu Cys Arg Gly Ser Pro Leu Val Val Ile Ser
	245 250 255	435 440 445
	5 Ser Lys Ser Ser Ala Glu Val Ile Ala Gln Ala Arg Lys Lys Gly Thr	5 Gin Gly Lys Ile Val Leu Glu Asp Gly Thr Leu His Val Thr Glu Gly
	260 265 270	450 455 460
	Val Val Tyr Gly Glu Pro Ile Thr Ala Ser Leu Gly Thr Asp Gly Ser	Ser Gly Arg Tyr Ile Pro Arg Lys Pro Phe Pro Asp Phe Vel Tyr Lys
	275 . 280 285	465 470 475 480
	His Tyr Trp Ser Lys Asn Trp Ala Lys Ala Ala Ala Phe Val Thr Ser	Arg ile Lys Ala Arg Ser Arg Leu Ala Glu Leu Arg Gly Val Pro Arg
01	290 295 . 300	10 485 490 495
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	Glu Gly Thr Asn Gly Thr Glu Glu Arg Met Ser Val Ile Trp Asp Lys	Gln Ile Asp Asp Asn Ile Pro Arg Arg Thr Gln Arg Ile Val Ala
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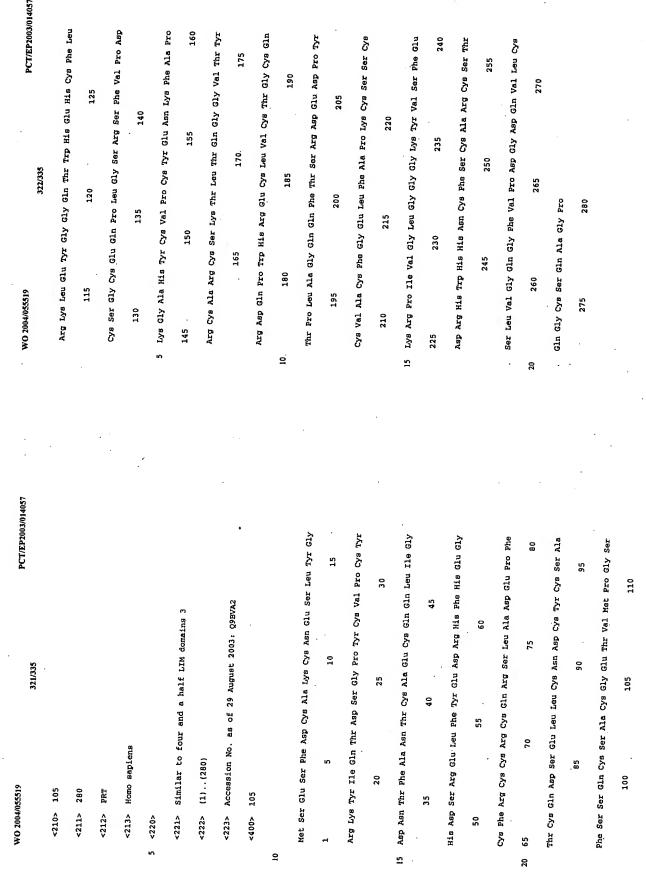
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•	Asp Glu His Gly Tyr]	Asp Glu His Gly Tyr Ile Ser Arg Cys Phe Thr Arg Lys Tyr Thr Leu	Thr Leu	Leu Ala Lys Pro Leu Val Lys Phe Ile Gln Gln Thr Tyr Pro Ser Gly
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••	145 1	150 155	160	35 40 45
15	ily Thr Leu Thr Val G	Gly Thr Leu Thr Val Glu Ala Pro Met Pro Lys Leu Ala Thr Gln Ser	Gln Ser : 15	5 Leu Arg Arg Ala Ala Val Gly Arg Pro Leu Asp Lys His Glu Gly Ala
	165	170 1	175	50 55 60
~	sn Glu Ile Thr Ile P	Asn Glu ile Thr ile Pro Val Thr Phe Glu Ser Arg Ala Gln Leu Gly	eu Gly	Leu Glu Thr Leu Leu Arg Tyr Tyr Asp Gln Ile Cys Ser Ile Glu Pro
·	180	185 190		. 65 70 75 80
	ly Pro Glu Ala Ala L	Gly Pro Glu Ala Ala Lys Ser Asp Glu Thr Ala Ala Lys		Lys Phe Pro Phe Ser Glu Asn Gln Ile Cys Leu Thr Phe Thr Trp Lys
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Gly Leu Lys Ile Ala Ala Lys His Tyr Gln Phe Ala Ser Gly Ala Phe	Ile Ser Gln Lys
145 150 155 160	340 345 350
Leu His Ile Lys Glu Thr Val Leu Ser Ala Leu Ser Arg Glu Pro Thr	5 Asp Leu Phe Glu Lys Met Val Pro Val Ser Val Gln Gln Ser Leu Ala
165	356 . 096 . 356
Val Asp Ile Ser Pro Asp Thr Val Gly Thr Leu Ser Leu Ile Met Leu	Ala Tyr Asn Gln Arg Lys Ala Asp Leu Val Asn Arg Ser Ile Ala Gln
180 185 190	370 375 380
Ala Gln Ala Gln Val Phe Phe Leu Lys Ala Thr Arg Asp Lys Met	Met Arg Glu Ala Thr Thr Leu Ala Asn Gly Val Leu Ala Ser Leu Asn
195 200 . 205	10 385 390 395 400
Lys Asp Ala Ile Ile Ala Lys Leu Ala Asn Gln Ala Ala Asp Tyr Phe	Leu Pro Ala Ala Ile Glu Asp Val Ser Gly Asp Thr Val Pro Gln Ser
210 215 220	405 410 415
Gly Asp Ala Phe Lys Gln Cys Gln Tyr Lys Asp Thr Leu Pro Lys Glu	11e Leu Thr Lys Ser Arg Ser Val 11e Glu Gln Gly Gly 11e Gln Thr
225 230 235 240	420 425 430
Val Phe Pro Val Leu Ala Ala Lys His Cys Ile Met Gln Ala Asn Ala	15 Val Asp Gln Leu Ile Lys Glu Leu Pro Glu Leu Gln Arg Asn Arg
245 250 . 255	435 440 445
Glu Tyr His Gln Ser Ile Leu Ala Lys Gln Gln Lys Lys Phe Gly Glu	Glu Ile Leu Asp Glu Ser Leu Arg Leu Leu Asp Glu Glu Ala Thr
260 265 270	450 . 455 460
Glu Ile Ala Arg Leu Gin His Ala Ala Glu Leu Ile Lys Thr Val Ala	Asp Asn Asp Leu Arg Ala Lys Phe Lys Glu Arg Trp Gln Arg Thr Pro
275 280 285	20 465 470 475 480
Ser Arg Tyr Asp Glu Tyr Val Asn Val Lys Asp Phe Ser Asp Lys Ile	Ser Asn Glu Leu Tyr Lys Pro Leu Arg Ala Glu Gly Thr Asn Phe Arg
290 295 300.	485 490 495
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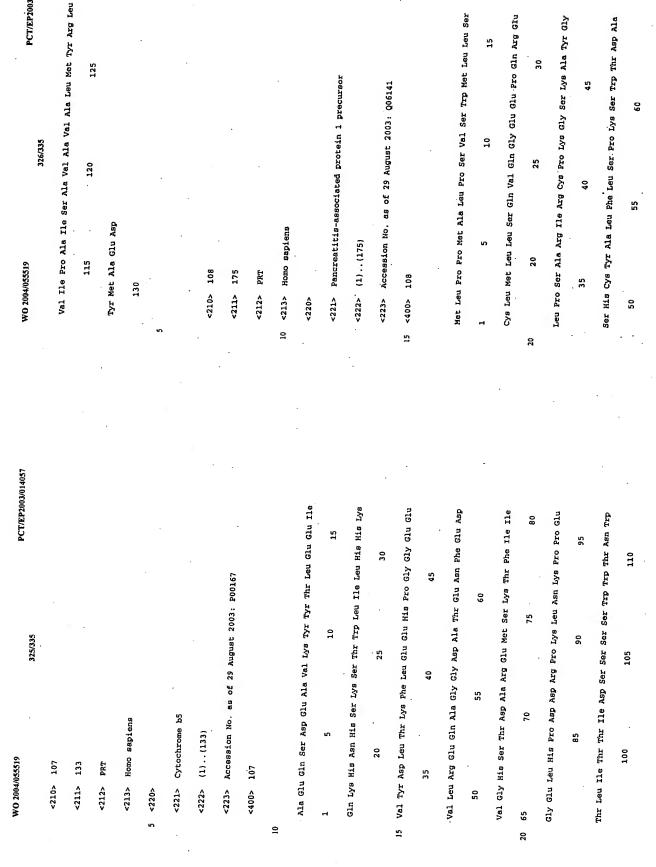
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S15 S20 S15	•	Tyr Gln Ser His Arg Asp Thr Ile Val Leu Leu Cys Lys Pro Glu Pro	Leu Lys Asp Leu Gln Gln Ser Ile Ala Arg Glu Pro Ser Ala Pro
Giu Veu Aen Ala Ala 11e Pro Ser Ala Ann Pro Ala Lye Thr Het Gin 543 543 545 546 Glu Vel Lye Lye Glu Vel Vel Ann Vel Leu Lye Ser Leu Leu Ser Asn Leu Aap 545 546 Glu Vel Lye Lye Glu Ary Glu Gly Leu Glu Aen Aap Leu Lye Ser Vel 555 Aen Phe Aap Met Thr Ser Lye Phe Leu Thr Ala Leu Ala Glu Aap Gly 560 580 580 580 580 580 680 680		520	705 710 715 720
5 diy Ser Ciu val Val Am Val Leu Lya Ser Leu Leu Ser Aan Leu Aap 545 546 Glu Val Lya Lya Glu Arg Glu Gly Leu Glu Aen Aep Leu Lya Ser Val 565 Asn Phe Asp Net Thi Ser Lya Phe Leu Thi Ala Leu Ala Glu Aap Gly 580 580 580 580 580 580 580 58		Glu Leu Asn Ala Ala Ile Pro Ser Ala Asn Pro Ala Lys Thr Met Gln	Ser lle Pro Thr Pro Ala Tyr Gin Ser Ser Pro Ala Gly Gly His Mis
Start Circ val val Asm val Lew Lys Ser Lew Lew Ser Asm Lew Asp S55 S60		535	725 730 735
Sign Sign			Pro Thr Pro Pro Thr Pro Ala Pro Arg Thr Met Pro Pro Thr
Second 1		545 550 555 560	740 745 750 750
Asn Phe Asp Met This Ser Lys Phe Leu This Ala Calu Ala Cliu Asp Cly 580 580 580 580 580 580 580 58		Glu Val Lys Lys Glu Arg Glu Gly Leu Glu Asn Asp Leu Lys Ser Val	Gin Pro Pro Als Arg Pro Pro Pro Val Leu Pro Ala Asn Arg Ala
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1 1 2 2 2 2 2 2 2 2		Asn Phe Asp Met Thr Ser Lys Phe Leu Thr Ala Leu Ala Gln Asp Gly	Pro Ser Ala Thr Ala Pro Ser Pro Val Gly Ala Gly Thr Ala Ala Pro
Val 11e Asn Glu Glu Ala Leu Ser Val Thr Glu Leu Asp Arg Val Tyr 595 600 605 Gly Gly Leu Thr Thr Lys Val Gln Glu Ser Leu Lys Lys Gln Glu Gly 610 620 620 Leu Leu Lys Asn Ile Gln Val Ser His Gln Glu Phe Ser Lys Met Lys 640 615 640 Gln Ser Asn Asn Glu Ala Asn Leu Arg Glu Glu Val Leu Lys Asn Leu 655 655 Ala Thr Ala Tyr Asp Asn Phe Val Glu Leu Val Ala Asn Leu Lys Glu 665 670 Gly Thr Lys Phe Tyr Asn Glu Leu Thr Glu Ile Leu Val Arg Phe Gln 685 Abn Lys Cys Ser Asp Ile Val Phe Ala Arg Lys Thr Glu Arg Asp Glu 685	11	580 585 590	
61y G1y Leu Thr Thr Lys Val Gln Glu Ser Leu Lys Lys Gln Glu Gly 610 610 611 612 612 613 613 614 615 615 616 617 618 618 619 619 619 619 610 610 610 610		Vel Ile Asn Glu Glu Ala Leu Ser Val Thr Glu Leu Asp Arg Val Tyr	Ala Pro Ser Gln Thr Pro Gly Ser Ala Pro Pro Pro Gln Ala Gln Cl.
Gly Gly Leu Thr Thr Lys Val Gln Glu Ser Leu Lys Gln Glu Gly 610 Leu Leu Lys Asn Ile Gln Val Ser His Gln Glu Phe Ser Lys Met Lys 625 Gln Ser Asn Asn Glu Ala Asn Leu Arg Glu Glu Val Leu Lys Asn Leu 645 Ala Thr Ala Tyr Asp Asn Phe Val Glu Leu Val Ala Asn Leu Lys Glu 660 Gly Thr Lys Phe Tyr Asn Glu Leu Thr Glu Ile Leu Val Arg Phe Gln 675 Asn Lys Cys Ser Asp Ile Val Phe Ala Arg Lys Thr Glu Arg Asp Glu 685 Asn Lys Cys Ser Asp Ile Val Phe Ala Arg Lys Thr Glu Arg Asp Glu		909	785 790 795 800
610 615 620 Leu Leu Lys Asn Ile Gln Val Ser His Gln Glu Phe Ser Lyg Met Lyg 625 Gln Ser Asn Asn Glu Ala Asn Leu Arg Glu Glu Val Leu Lys Asn Leu 645 Ala Thr Ala Tyr Asp Asn Phe Val Glu Leu Val Ala Asn Leu Lys Glu 660 Gly Thr Lyg Phe Tyr Asn Glu Leu Thr Glu Ile Leu Val Arg Phe Gln 675 Asn Lys Cys Ser Asp Ile Val Phe Ala Arg Lys Thr Glu Arg Asp Glu		Gly Gly Leu Thr Thr Lys Val Gln Glu Ser Leu Lys Lys Gln Glu Gly	Tyr Cys Gln Met
15 16 12 13 15 15 15 15 15 15 15		615	805 810 815
Gln Ser Asn Asn Glu Ala Asn Leu Arg Glu Glu Val Leu Lys Asn Leu 645 650 655 Ala Thr Ala Tyr Asp Asn Phe Val Glu Leu Val Ala Asn Leu Lys Glu 660 615 617 618 619 619 619 619 619 619 619 619 619 619	15	Leu Leu Lys Asn 11e Gln Val Ser His Gln Glu Phe Ser Lys Met Lys	Met Pro Met Gly Tyr Asn Pro Tyr Ala Tyr Gly Gln Tyr Asn.
Gin Ser Asn Asn Glu Ala Asn Leu Arg Glu Glu Val Leu Lys Asn Leu 645 Ala Thr Ala Tyr Asp Asn Phe Val Glu Leu Val Ala Asn Leu Lys Glu 660 Gly Thr Lys Phe Tyr Asn Glu Leu Thr Glu Ile Leu Val Arg Phe Gln 678 Asn Lys Cys Ser Asp Ile Val Phe Ala Arg Lys Thr Glu Arg Asp Glu		630 635	820 825 830
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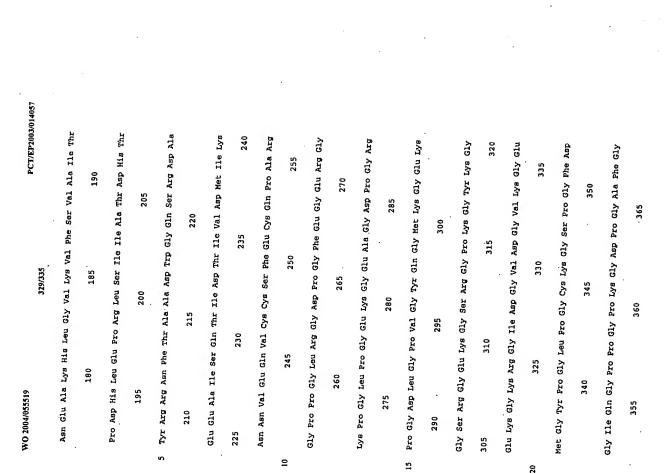
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Arg Lys Tyr 11e Gln Thr Asp Ser Gly Pro Tyr Cy	'yr Cys Val Pro Cys Tyr	Cys Val Ala Cys Phe Gly Glu Leu Phe Ala Pro Lys Cys Ser Ser Cys
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His Asp Ser Arg Glu Leu Phe Tyr Glu Asp Arg His Phe His Glu Gly	rg His Phe His Glu Gly	Asp Arg His Try His His Asn Cys Phe Thr Cys Asp Arg Cys Ser Asn
55 ,		245 250 255
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Thr Arg Gln Asp Ser Glu Leu Leu Cys Asn Asp Cys	sp Cys Tyr Cys Ser Ala	Gin Gly Cys Ser Gin Ala Gly Pro
. 85		275 280
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	<221> Collagen alpha 1(VI) chain precursor	145 150 155 160
	<222> (1)(1028)	Pro Leu Glu Gly Tyr Lys Glu Pro Cys Gly Gly Leu Glu Asp Ala Val
	<223> Accession No. as of 29 August 2003: P12109	165 170 175



Gly

Gly Pro Gln Gly Asp Gln Gly Arg Glu Gly Pro Val Gly Val Pro

Asp Pro Gly Glu Ala Gly Pro Ile Gly Pro Lys Gly Tyr Arg Gly Asp

Glu Gly Pro Pro Gly Ser Glu Gly Ala Arg Gly Ala Pro Gly Pro Ala

.

Gly Pro Pro Gly Asp Pro Gly Leu Met Gly Glu Arg Gly Glu Asp Gly

Pro

Pro Ala Gly Asn Gly Thr Glu Gly Phe Pro Gly Phe Pro Gly Tyr

Gly Asn Arg Gly Ala Pro Gly Ile Asn Gly Thr Lys Gly Tyr Pro Gly

Leu Lys Gly Asp Glu Gly Glu Ala Gly Asp Pro Gly Asp Asp Asn Asn

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Leu Lys Gly Glu Lys Gly Glu Pro Gly Ala Asp Gly Glu Ala Gly Arg

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Pro Gly Ala Arg Gly Pro Ser Gly Asp Glu Gly Pro Ala Gly Glu Pro

Gly Pro Pro Gly Glu Lys Gly Glu Ala Gly Asp Glu Gly Asn Pro Gly

Pro Asp Gly Ala Pro Gly Glu Arg Gly Gly Pro Gly Glu Arg Gly Pro

Arg Gly Thr Pro Gly Pro Arg Gly Pro Arg Gly Asp Pro Gly Glu Ala

W0 2	WO 2004/055519	331/335	PCT/EP2003/014057		WO 2004/055519	Pp. 332/338	PCT/EP2003/01
Asi	ile Ala Pro A	Asp ile Ala Pro Arg Gly Val Lys Gly Ala Lys	ys Gly Tyr Arg Gly Pro		Ser Val Gly Ile Lys	Ser Val Gly Ile Lys Asp Val Phe Asp Phe Ile Pro Gly Ser Asp Gln	: Asp Gln
	iń.	565 570	575		755	765	
G1,	1 Gly Pro Gln G	Glu Gly Pro Gln Gly Pro Pro Gly His Gln Gly Pro Pro Gly Pro Asp	ly Pro Pro Gly Pro Asp		Leu Asn Val Ile Ser (Leu Asn Val Ile Ser Cys Gln Gly Leu Ala Pro Ser Gln Gly Arg Pro	Arg Pro
	580	. 585	290		. 077	775 . 780	
5 Glu	. Cys Glu Ile L	Glu Cys Glu Ile Leu Asp Ile Ile Met Lys Met Cys	et Cys Ser Cys Glu		5 Gly Leu Ser Leu Val 1	Gly Leu Ser Leu Val Lys Glu Asn Tyr Ala Glu Leu Leu Glu Asp Ala	Asp Ala
	595	009	605	•	785	790 795	800
ζζ	Lys Сув Gly Pl	Cys Lys Cys Gly Pro lle Asp Leu Leu Phe Val Leu Asp Ser	al Leu Asp Ser Ser Glu		Phe Leu Lys Asn Val 1	Phe Leu Lys Asn Val Thr Ala Gln Ile Cys Ile Asp Lys Lys Cys Pro	Cys Pro
	010	615	620		805	810	815
Ser	Ile Gly Leu Gl	Ser Ile Gly Leu Gln Asn Phe Glu Ile Ala Lys Asp Phe Val Val Lys	ys Asp Phe Val Val Lys		Asp Tyr Thr Cys Pro 1	Asp Tyr Thr Cys Pro Ile Thr Phe Ser Ser Pro Ala Asp Ile Thr Ile	Thr Ile
10 625		. 089	635 640	. 10	. 820	825 830	
Val	Ile Asp Arg Le	Val ile Asp Arg Leu Ser Arg Asp Glu Leu Val Ly	al Lys Phe Glu Pro Gly		Leu Leu Asp Gly Ser A	Leu Leu Asp Gly Ser Ala Ser Val Gly Ser His Asn Phe Asp Thr Thr	Thr Thr
	64	645 650	655		835	840 845	
Gln	Ser Tyr Ala Gl	Gln Ser Tyr Ala Gly Val Val Gln Tyr Ser His.Ser Gln Met Gln Glu	ls.Ser Gln Met Gln Glu		Lys Arg Phe Ala Lys A	Lys Arg Phe Ala Lys Arg Leu Ala Glu Arg Phe Leu Thr Ala Gly Arg	Gly Arg
•	099	665	670	•	. 850		
15 His	Val Ser Leu Ar	His Val Ser Leu Arg Ser Pro Ser Ile Arg Asn Val Gln Glu Leu Lys	n Val Gln Glu Leu Lys			Thr Asp Pro Ala His Asp Val Arg Val Ala Val Val Gln Tyr Ser Gly	Ser Gly
	675	089 .	. 589		865	870 875	. 880
Glu	Ala Ile Lys Se	Glu Ala Ile Lys Ser Leu Gln Trp Met Ala Gly Gly Thr Phe Thr Gly	y Gly Thr Phe Thr Gly		Thr Gly Gln Gln Arg P	Gly Gln Gln Arg Pro Glu Arg Ala Ser Leu Gln Phe Leu Gln Agn	Gln Asn
	069	695	700		885	068	895
Glu	Ala Leu Gln Ty.	Glu Ala Leu Gln Tyr Thr Arg Asp Gln Leu Leu Pro Pro Ser Pro Asn	u Pro Pro Ser Pro Asn		Tyr Thr Ala Leu Ala S	Tyr Thr Ala Leu Ala Ser Ala Val Asp Ala Met Asp Phe Ile Asn Asp	Авп Авр
20 705		710 715	5 720	20		905 910	
. Asn	Arg Ile Ala Le	Asn Arg Ile Ala Leu Vel Ile Thr Asp Gly Arg Ser Asp Thr Gln Arg	g Ser Asp Thr Gln Arg		Ala Thr Asp Val Asn A	Ala Thr Asp Val Asn Asp Ala Leu Gly Tyr Val Thr Arg Phe Tyr Arg	Tyr Arg
	. 725	5 730	735		915	920 . 925	
Asp	Thr Thr Pro Let	Asp Thr Thr Pro Leu Asn Val Leu Cys Ser Pro Gly Ile Gln Val Val	o Gly Ile Gln Val Val		Glu Ala Ser Ser Gly Al	Glu Ala Ser Ser Gly Ala Ala Lys Lys Arg Leu Leu Leu Phe Ser Asp	Ser Asp
٠.	740	745	750		930	935 940	

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200 200	333/335 PCT/EP2003/014057	WO 2004/055519 PCT/(PB2002202
345 950 955 960 Glu Ala Gin Arg Ala Giy Ile Glu Lie Phe Val Val Val Ciy Arg 965 970 975 Glu Ala Giy Eco His Ile Arg Val Leu Val Thr Gly Lya Thr Ala 980 985 990 Glu Tyr Asp Val Pro Tyr Gly Gly Ser His Leu Phe Arg. Val Bro Ser 995 1000 1005 Tyr Gly Ala Leu Leu Arg Gly Val Phe His Gln Thr Val Ser Arg 1010 1020 1020 1020 10 6 1020 110 1025 1103 1210 110 1210 110 1210 1210 1210 121	Glv kan ser nin in	
Glu Ala Glu Arg Ala Gly Ile Glu Ile Phe Val Val Val Oly Arg 965 Glu Ala Glu Pro His Ile Arg Val Leu Val Thr Gly Lys Thr Ala 980 985 990 Glu 7yr Aug Val Pro 7yr Gly Glu Ser His Leu Phe Arg Val Pro Ser 985 990 1005 1007 1007 1008 1008 1008 1008 2100 2109	521 J. J. Ala Thr Pro Ala Ala Ile Glu Lys Ala Val	Met Ser Leu Ser Ala Phe Thr Leu Phe Leu Ala Leu Tle ch. ch.
Gin Ais Gin Arg Aig Giy Ile Giu Ile Phe Val Val Val Ciy Arg 955 970 975 Gin Val Asm Glu Pro His Ila Arg Val Leu Val Thr Giy Lyu Thr Aig 980 985 980 985 1000 1005 1000 1015 1020 1	945 . 950 955 960	1 s
10 10 10 10 10 10 10 10	Glu Ala Gin Arg Ala Gly Ile Glu Ile Phe Val Val Val Gly Arg	Ser Gly Gln five from from from from from from from from
Oth Val Amn Glu Pro His Ile Arg Val Leu Val Thr Gly Lyg Thr Ala 990 Glu Tyr Amp Val Pro Tyr Gly Glu Ser His Leu Phe Arg Val Pro Ser 990 Glu Tyr Amp Val Pro Tyr Gly Glu Ser His Leu Phe Arg Val Pro Ser 995 Tyr Gln Ala Leu Leu Arg Gly Val Phe His Gln Thr Val Ser Arg 1010 Lyg Val Ala Leu Gly 1015 1020 1020 1020 1021 1025 1020 103 104 105 105 105 107 108 109 109 109 109 109 109 100 1	965 970 975	, 131 ABP 19T ABP Phe Pro Leu Ser Ile Tyr Gly Gln
986 986 995 990 1000 1005 1005 1005 1005 1005 1005 10	Gln Val Asn Glu Pro His Ile Arg Val Leu Val Thr Gly Lys Thr Ala	
797 Asp Val Pro Tyr Gly Glu Ser His Leu Phe Arg Val Pro Ser 1000 1005 1100 1015 1020 1010 1015 1020 1010 101	980 986	
1005 210 Ala Leu Leu Arg Gly Val Phe His Gln Thr Val Ser Arg 1010 1015 1020 1016 1017 1010 110 110 110 110	Glu Tyr Asp Val Pro Tyr Gly Glu Ser His Leu Phe Arg. Val pro car	35 40 45
100 1015 1020 10 1015 1020 1015 1020 10 101 100 1015 1020 10 110 110 110 110 110 110 110 110 11	1000 366	ser Ala Met Tyr Cys Asp Glu Leu Lys Leu Lys Ser Val Pro Met Val
100 101 1020 1035 110 110 110 110 110 110 1110 1110	byr Gln Ala Leu Leu Arg Gly Val Phe His Gln Thr Val Ser Arm	50 55 60
110 110 110 1338 PRT Homo sapiens (1)(338) Accession No. as of 29 August 2003: P51884 110 S55	1010 1015 1020	
110 110 110 110 110 110 110 110 110 12 13 14 Homo sapiens 17 Tumican precursor (1)(338) 110 110 110		
110 138 PRT Homo sapiens Homo sapiens 15 16 17 17 18 110 19 10 110	1025	Ile Asp Glu Lys Ala Phe Glu Asn Val Thr Asp Leu Gln Trp Leu Ile
110 PRT Homo sapiens 15 Accession No. as of 29 August 2003: P51884 110		06
110 338 PRT Homo sapiens Lumican precursor [1](338) [1](338) Accession No. as of 29 August 2003: P51884 110		Leu Asp His Asn Leu Glu Asn Ser Lys Ile Lys Gly Arg Val Phe
1318 PRT Homo sapiens Lumican precursor [1](338) Accession No. as of 29 August 2003: P51884 110		100 105 110
Homo sapiens Lumican precursor [1](338) Accession No. as of 29 August 2003: P51884		
Homo sapiens Lumican precursor [1](338) Accession No. as of 29 August 2003: P51884		120
Lumican precursor (1)(338) Accession No. as of 29 August 2003; P51884	13> Homo sapiens	•
Lumican precursor (1)(338) Accession No. as of 29 August 2003; P51884	<02	135
20 (1)(338) Accession No. as of 29 August 2003. P51884	11> Lunican procures.	Thr His Asn Lys Ile Thr Lys Leu Gly Ser Phe Glu Gly Leu Val Asn
Accession No. as of 29 August 2003: P51884	(2> (1) . (338)	
110	3> Accession No. as of 29 August 2003: P51884	Leu Thr Phe Ile His Leu Gln His Asn Arg Leu Lys Glu Asp Ala Val
Ser Ala Ala Phe Lys Gly Leu Lys Ser Leu Glu Tyr Leu Asp Leu Ser	0> 110	170
		Ser Ala Ala Phe Lys Gly Leu Lys Ser Leu Glu Tyr Leu Asp Leu Ser

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Phe Asn Gln Ile Ala Arg Leu Pro Ser Gly Leu Pro Val Ser Leu Leu

Thr Leu Tyr Leu Asp Asn Asn Lys Ile Ser Asn Ile Pro Asp Glu Tyr

5 Phe Lys Arg Phe Asn Ala Leu Gln Tyr Leu Arg Leu Ser His Asn Glu

Leu Ala Asp Ser Gly Ile Pro Gly Asn Ser Phe Asn Val Ser Ser Leu

Val Glu Leu Asp Leu Ser Tyr Asn Lys Leu Lys Asn Ile Pro Thr Val

Asn Glu Asn Leu Glu Asn Tyr Tyr Leu Glu Val Asn Gln Leu Glu Lys

Phe Asp Ile Lys Ser Phe Cys Lys Ile Leu Gly Pro Leu Ser Tyr Ser

15 Lys lle Lys His Leu Arg Leu Asp Gly Asn Arg lle Ser Glu Thr Ser

Leu Pro Pro Asp Met Tyr Glu Cys Leu Arg Val Ala Asn Glu Val Thr

Leu Asn

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